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Study protocol for a feasibility study of an internet-administered, guided, CBT-based, self-help intervention (ENGAGE) for parents of children previously treated for cancer

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ABSTRACT

Introduction: A subgroup of parents of children previously treated for cancer report long-term psychological distress after end of treatment. However, needs for psychological support are commonly unmet and there is a lack of evidence-based treatments tailored to the specific needs of this population. An internet-administered, guided, cognitive-behavioural therapy (CBT) based, self-help intervention (ENGAGE) for parents of children previously treated for cancer, may provide a solution. The aim is to examine methodological, procedural, and clinical uncertainties regarding the intervention ENGAGE and associated study procedures such as estimates of likely recruitment and retention rates, and the feasibility and acceptability of instruments, data collection procedures, and the feasibility and acceptability of the intervention.

Methods and analysis: The study has an uncontrolled, within group, baseline-, post-treatment (12 weeks), and six-month follow-up design with an embedded qualitative and quantitative process evaluation. Potential participants are parents of children previously treated for cancer, living in Sweden, recruited via their child's personal identification number (via the Swedish Childhood Cancer Registry and the Swedish Tax Agency). Parents are invited randomly with information packs sent to home addresses. Further interest in participating can be registered via information on relevant websites. The study aims to recruit 50 parents who will receive the intervention ENGAGE which is designed to be delivered over a 10-week period, and comprises one introductory chapter followed by up to 10 intervention modules addressing key concerns identified for the population.

Ethics and dissemination: The Regional Ethical Review Board in Uppsala, Sweden has granted approval for the study (Dnr: 2017/527). Results will be disseminated to relevant healthcare and patient communities, in peer-reviewed and popular science journals, and at scientific and clinical conferences.

Keywords: Parents; eHealth; Depression; Anxiety; Clinical trial

Trial registration number: ISRCTN57233429

ARTICLE SUMMARY

Strengths and limitations of this study

- Development of the internet-administered, guided, CBT based, self-help intervention ENGAGE has included not only consulting of theoretical literature and clinical expertise but also extensive involvement of end-users by means of Participatory Action Research.
- This study will examine the feasibility and acceptability of the intervention ENGAGE alongside planned study procedures for a controlled trial.
- This study will examine methodological, procedural, and clinical challenges to revise and refine the intervention ENGAGE, study design, and planned procedures prior to a controlled trial following established feasibility study progression criteria.
- This study is limited to examining the feasibility and acceptability of intervention delivery within a university setting and does not examine the feasibility of implementation within a real-life healthcare context.

INTRODUCTION

Most children diagnosed with cancer survive their disease.[1] However, childhood cancer impacts on the whole family from diagnosis into survivorship.[2] For parents, a child's treatment completion is not only an important milestone but also a period of psychological vulnerability.[3, 4] A subgroup report negative long-term psychological consequences years after treatment completion.[4-7] However, there is a lack of evidence-based psychological interventions for parents who experience distress in relation to a child's cancer disease after end of treatment. Recently published guidelines, informing how children diagnosed with cancer and their family members should be cared for, recommend referrals to appropriate therapeutic support into long-term survivorship.[8] However, significant challenges remain regarding provision of such support. We have reported an unmet need of psychological support among parents of children previously treated for cancer.[9] The results are in line with findings from an Australian study showing that formal psychological support was difficult to access and rarely received by parents after completion of cancer treatment.[10] Factors related to staff availability, models of assessment and delivery of services, and size and location of paediatric cancer units hindered provision of support.

Using the internet to deliver psychological support may increase access to support and represent an alternative model of psychological support delivery for parents of children previously treated for cancer. We have shown an internet-administered psychological, self-help intervention to be effective in reducing symptoms of anxiety, depression, and posttraumatic stress (PTSS) among parents of children recently diagnosed with cancer,[11] with improvements maintained at one year follow-up.[12] However, challenges with recruitment and attrition were encountered, indicating that end-user involvement in the development of interventions, alongside informing study procedures to test and evaluate interventions, may be essential for intervention research within this population.[13] Research suggests internet-administered, self-help interventions should be developed with the target population in mind,[14] with lower levels of acceptability found for internet-administered interventions not developed for a specific population.[15] Additionally, recruitment and adherence rates may improve if the perspective of the population is adopted.[16] Finally, there is currently a lack of evidence-based psychological support for parents who experience distress in relation to a child's cancer disease after successful cancer treatment, despite clear findings showing that a subgroup of parents report long-term psychological distress.[4, 5, 9]

The aim is to examine the feasibility and acceptability of the internet-administered, CBT-based, guided, self-help intervention ENGAGE for parents of children previously treated for cancer and the study procedures for a future controlled trial. We have undertaken a programme of Phase I (development) research, following the Medical Research Council (MRC) complex interventions framework [17] to inform the development of the intervention. First, a systematic review of cancer-related long-term negative and positive psychological effects for parents of childhood cancer survivors was conducted,[4] with results used to inform the development and piloting of a face-to-face CBT based intervention. The intervention was successful, resulting in improvements in symptoms of anxiety, depression, and PTSS (d=0.65-0.92) at post-treatment and three-month follow-up.[18] Subsequently a Participatory Action Research (PAR)[19] approach was adopted to inform the design, content, and delivery of the intervention in collaboration with parent and expert research partners.[20] Finally, an online survey study, utilizing a population-based cross-sectional design, further examined preferences regarding study procedures e.g. type of controlled design and mode of recruitment (letter versus postal card).["Personal communication" by J Woodford, 20180406] Parents of children who had completed cancer treatment were invited to complete the survey,

with 32% (n=112) of 350 responding. Findings indicated no differences in response rate between mode of invitation (n=59 [34%] letter, n=53 [30%] postal card; p=0.447). Overall, parents perceived proposed study procedures (e.g., receipt of initial study information via postal letter, presentation of detailed study information online, via text and informational video, randomisation) and the receipt of internet-administered psychological support as acceptable. These findings informed the recruitment and provision of study information procedures to be further examined in the present feasibility study.

The key feasibility outcomes examined via the proposed protocol concern methodological, procedural, and clinical uncertainties,[21-23] including: (1) estimates of likely recruitment and retention rates; (2) feasibility and acceptability of data collection instruments and data collection procedures; and (3) feasibility and acceptability of the intervention. In line with standard feasibility study objectives [21] improvements regarding clinical outcomes are not examined at this stage. However, an embedded qualitative process evaluation [24] will be used to examine the: (1) acceptability of intervention; (2) self-reported psychological needs; (3) parents' healthcare utilization and productivity losses related to the child's cancer disease; (4) potential mechanisms of change; and (5) the impact of the intervention on parents' difficulties.

METHODS AND ANALYSIS

This protocol (version 1, 14/03/2018) is reported according to guidelines presented in the CONSORT 2010 statement extension for randomized pilot and feasibility studies [23] and clinical trial protocols [25].

Design

The study has an uncontrolled, within-group, baseline-, post-treatment (12 weeks), and six-month follow-up design with an embedded qualitative and quantitative process evaluation. All participants will receive the internet-administered, CBT based, self-help intervention ENGAGE, guided by an e-therapist for 10 weeks, comprising one introductory chapter followed by up to 10 treatment modules addressing key concerns identified for the population.

Eligibility criteria

Parents/caregivers (from here referred to as parents or participants) will be included according to: (1) parent of a child diagnosed with cancer when 0-18 years who has completed cancer treatment three months to five years previously; (2) resides in Sweden; (3) able to read and understand text in Swedish; (4) has access to e-mail, the internet, and a mobile telephone and/or Bank ID (a citizen authentication system used in Sweden); and (5) self-reports a need for psychological support related to the child's cancer disease and treatment. The following exclusion criteria will be used: (1) self-reported or clinician assessed (based on the M.I.N.I neuropsychiatric interview);[26] symptoms of a severe and enduring mental health difficulty; (2) self-reported or clinician assessed (based on the M.I.N.I neuropsychiatric interview);[26] misuse of alcohol, street drugs, and/or prescription medication; (3) acutely suicidal; and (4) currently attending psychological treatment. Those excluded due to a severe and enduring mental health difficulty, substance misuse, and/or acute suicidality will be guided to appropriate healthcare services.

Sample size

The eligible population includes approximately 2400 parents, with around 30% (720/2400) expected to experience a need of psychological support.[9] Approximately 30% of these (216/720) are expected to potentially consent.[11, 12, 18] Following recommendations of

sample sizes of 50-60 being appropriate to assess feasibility outcomes and estimate sample size for a definite trial [27] we aim to recruit a sample of 50 participants. If 50 are included, we will be able to estimate a participation rate of 90% within a 95% confidence interval of +/- 8%.

Recruitment

Participants will be recruited using two approaches: (A) Children's personal identification numbers will be obtained from the Swedish Childhood Cancer Registry (National Quality Registry, initiated in 1982) and linked to parents' names and addresses via NAVET, a registry held by the Swedish Tax Agency. Parents will be invited to participate randomly by the research team, using blocks of 100 until the target number of 50 has been reached. Prior to inviting parents into the study, the most up to date information concerning whether children are currently living or deceased will be checked via the telephone by a member of the research team with Swedish Tax Agency. A study information pack will be sent to home addresses, including brief information about the study and a www-address to a secure website, the U-CARE-portal (Portal). Potential participants will be able to access information via the Portal, with study information presented in text and video format. They will be able to either register interest in the study, or opt out of the study, by: (1) completing an online form via the Portal; (2) returning a reply slip using a freepost envelope; (3) telephoning the research team; or (4) e-mailing the research team. Given the use of reminders improves recruitment rates,[28] telephone numbers of those who do not respond to the research team, within four weeks of sending the postal study information pack, will be identified via internet search engines. A member of the research team will telephone all non-responders. The purpose will be to confirm receipt of the study invitation pack and answer any questions the parent may have regarding the study. In cases whereby the telephone call is not answered a maximum of four additional telephone call attempts to establish contact will be made over the following four weeks. The study information sheet will clearly specify that a member of the research team will attempt to telephone call non-responders, with parents provided with the aforementioned methods of opting out of the study should they not wish to receive a telephone call from a member of the research team. In cases whereby a participant's telephone number cannot be identified, a study information pack will be resent via the post with a reminder note added to the pack by the research team if no response is received within four weeks. (B) To raise awareness of the study, and potentially recruit to the study, advertisements will be placed on relevant social media sites and patient organizations' and interest groups' websites. People can receive more information about the study by telephoning or e-mailing the research team and register interest in the study by completing an online form via the Portal.

Reasons for non-participation

Parents deciding to opt out of further contact will be presented a short questionnaire (provided in paper format in information packs as well as online) listing possible reasons for non-participation as informed by previous research [29, 30] alongside an open-ended question for parents to provide further information and reasons for non-participation should they wish. Reasons for non-participation will be used to inform about barriers to recruitment and may provide data pertaining to the acceptability of the intervention and support offered. It will be made clear on both the paper and online questionnaire that the provision of reasons for non-participation is optional and parents do not need to report why they do not wish to participate if they would prefer not to.

Informed consent, screening, and baseline

Parents interested in participating will be asked to provide informed consent and contact

details via the Portal. Those who reply to the research team via a postal reply slip, telephone, or e-mail, will be called by a member of the research team, who will provide more information about the study. Those interested in participating will be asked to provide consent via the Portal. Parents who speak to a member of the research team and express interest in the study, but do not provide online consent within two weeks, will receive a telephone follow-up call and/or e-mail from a member of the research team. Where telephone calls are not answered, a maximum of five telephone calls will be made over a period of two weeks.

Parents providing informed consent will be contacted via telephone by a licensed psychologist for an eligibility interview with the purpose of confirming inclusion and exclusion criteria. If eligibility is confirmed, parents will be instructed to complete a baseline assessment via the Portal, with the option provided to complete the assessment via the telephone if preferred. In addition, a semi-structured interview will be completed at baseline over the telephone to gain a more detailed understanding e.g. concerning presenting problems and expectations for treatment. After the full baseline assessment is completed, parents will be provided access to the ENGAGE intervention via the Portal and will be allocated to an e-therapist. Participant flow through the study is illustrated in Figure 1.

Intervention

Content

Based on standard definitions of self-help [31] and taxonomies categorising levels of support, [32] ENGAGE can be described as an internet-administered, guided, CBT based, self-help intervention. ENGAGE includes written, audio, and video materials provided online via the Portal. The intervention includes (1) a short introductory chapter, followed by 10 CBT-based modules, with a brief overview of module content shown in Table 1; (2) an initial assessment session with an e-therapist via a video or telephone call during which the individual's problems and idiographic goals are formulated and parents are directed to the short introductory chapter and first module; and (3) weekly guidance from an e-therapist via the Portal (online written feedback). The intervention is designed to be delivered over a 10 weeks period, with parents encouraged to complete one module per week. However, the intervention will be accessible to parents for a 12 weeks period to provide flexibility regarding module completion and provision of e-therapist feedback and support. Module content is based on CBT techniques and is tailored towards key concerns and difficulties experienced by parents of children previously treated for cancer as informed by previous research.[3-5, 18] Each module includes psychoeducation alongside text, audio, and video material instructing parents in the use of specific CBT based techniques. Parents will be encouraged to complete weekly action plans and symptom questionnaires for each module which will be reviewed by the e-therapist. Further, modules include case vignettes, serving to clarify important treatment principles and help parents make connections between the material and their own experiences. Extensive efforts have been made to include 'common factors' within the intervention in order to establish, develop, and maintain a therapeutic alliance.[33] As such, the intervention has been developed to engage parents in materials by including statements of empathy, genuineness, and warmth, narratives referring to struggle and recovery, examples to help parents relate the text material to their own lives, and personal metaphors for emotional distress.[33]

Guidance from e-therapists

An e-therapist will guide the use of the intervention, following a structured support protocol developed specifically for the intervention. Guidance will consist of one video or telephone

assessment session, weekly online written support, and a mid-treatment video or telephone 'booster' session. Prior to the start of the intervention parents will be contacted by an

Table 1. Overview of the 10 modules included in the ENGAGE intervention.

	Title and description	Cognitive behavioural therapy strategies
Module 1	*"What have I experienced and where am I heading?"* *Processing and normalising the cancer experience and cancer-related distress, goal setting.*	Psychoeducation about typical reactions among parents of children previously treated for cancer. Setting intervention goals and long-term goals. Identifying challenging situations.
Module 2	*"Who takes care of me?"* *Analysing current problems using functional analysis. Principles of self-compassion.*	Introducing functional analysis. Psychoeducation about self-compassion and difficult life-events. Practicing self-compassion and functional analysis.
Module 3	*"Am I really here?"* *Mindfulness and acceptance-based strategies.*	Psychoeducation about emotions and mindfulness. Practicing noticing emotions and bodily sensations. Mindfulness and acceptance-based exercises and continue practicing functional analyses.
Module 4	*"Painful experiences"* *Exposure to painful memories and emotions and introducing skills to handle challenging situations and experiences.*	Psychoeducation about painful memories and emotions, and coping with fear of recurrence. Rationale for exposure techniques. Cognitive strategies for disengaging from patterns of unhelpful thinking. Continue practicing mindfulness and functional analyses.
Module 5	*"Looking inwards"* *Managing emotional avoidance through exposure.*	Intensifying exposure with specific focus on emotional avoidance through functional analyses and further exposure techniques. Continue practicing mindfulness.
Module 6	*"The worst I've ever experienced"* *Deepened focus on painful memories and emotions through expressive writing.*	Continued psychoeducation about painful memories and emotions. Reflecting on exposure exercises, reviewing goals from start of the programme. Continue practicing mindfulness. Expressive writing task.
Module 7	*"Back to life"* *Dealing with avoidance and painful emotions through behaviour activation and functional analyses.*	Reviewing goals and identifying challenging situations that remain, plan of action. Rationale for behavioural activation. Continuing exposure exercises.
Module 8	*"Be kind to yourself"* *Skills to better take care of oneself through principles of self-compassion and*	Continued psychoeducation about behaviour activation and self-compassion. Continue to practising self-compassion and behavioural activation.

	acceptance.	
Module 9	*"Becoming your own therapist"* *Applying new skills flexibly in everyday life.*	Psychoeducation about becoming one's own therapist. Identifying challenging situations that remain, review goals and form action plans. Focus on applying new skills in everyday life in a flexible manner.
Module 10	*"Where have I been and where am I heading now?"* *Progress review and skills for maintaining progress and set-backs.*	Reviewing the intervention, what worked better/worse, skills for maintaining change and handling set-backs.

e-therapist for the individual assessment session via video-call, lasting approximately 45 minutes. For parents not wanting to participate in a video-call there is also an option to complete the call via telephone. Parents will be able to communicate their current difficulties and the e-therapist will conduct an individually tailored behaviour analysis of the parent's main difficulties, collaboratively formulate idiographic treatment goals and introduce the intervention. Although parents will work independently with the intervention, e-therapists will provide weekly, and at-need, written support messages online via the Portal throughout the intervention. E-therapist guidance will include the provision of feedback on action plans, reinforcement of progress made, validating any difficulties experienced and providing assistance problem solving difficulties. E-therapists will provide encouragement, motivation, and guidance throughout the intervention, with parents able to contact their allocated e-therapist for additional guidance, via the Portal or telephone, should they experience a need. E-therapists will be obliged to respond to parents within one working day. Given the explorative nature of the study, no maximum time limit for support has been set, though based on previous experience [11, 12] we anticipate e-therapists will spend approximately 20-30 minutes per parent each week.

Parents will be provided a 'booster' session lasting 30-45 minutes, via video or telephone call, midway through the intervention. This session will be an opportunity to further assess any potential difficulties experienced with the ongoing work, provide additional guidance and assistance problem solving, alongside the provision of encouragement and motivation. Parents who do not log in, or show low activity in the intervention, will be contacted via text message, e-mail, and/or telephone, whichever is preferred by the parent and e-therapist.

E-therapists

E-therapists will be psychology programme students, in at least their 4th year of study, having completed a minimum of their first term of advanced studies in CBT, but will have not yet begun their prescribed practical service [i.e., praktisk tjänstgöring för psykologer/PTP]. Prior to study start, all e-therapists will participate in a one-day workshop to familiarise themselves with the treatment manual and support protocol, delivered by a licenced clinical psychologist. E-therapists will receive weekly group clinical supervision sessions focussing on case discussions, skills development, and at-need supervision by a licenced clinical psychologist with relevant experience of the population.

Optional support functions
Optional support functions within the Portal will include an online library containing information about CBT, self-help, literature suggestions, links to relevant websites as well as CBT exercises from the intervention. These materials will be available as downloadable text and audio files. In addition, all exercises used in the intervention will be accessible within the library for parents to revisit. As these functions are optional and not part of the treatment, parents will not receive any recommendations from their e-therapist regarding optimal level of engagement with these support functions.

Setting
Parents will receive guidance from e-therapists located at Uppsala University, Sweden. Due to the nature of the ENGAGE intervention being online, parents are anticipated to engage with the intervention in their own homes.

Outcome measures
Feasibility outcomes
Feasibility outcomes of interest relate to methodological, procedural, and clinical uncertainties [21-23] and examine recruitment rates, eligibility criteria, data collection, attrition, resources needed to complete the study and intervention, parents' adherence to the intervention, e-therapists' adherence to the support protocol and parents' acceptability of the intervention and study procedures. Feasibility outcomes assessed are shown in Table 2 alongside the associated progression criteria (where applicable). Progression criteria have been set to facilitate the interpretation of results and to inform whether to proceed to a definite trial after the feasibility study.

Sociodemographic and clinical variables
Data on child age, gender, diagnosis, date of first diagnosis, date of end of treatment (where available), and type of treatment will be obtained from the Swedish Childhood Cancer Registry. Self-report data on parent age, gender, education, employment status, ethnicity, relationship status, number of children, ages of children, current housing situation, previous psychological treatment, previous traumatic events, physical health, date of end of child's cancer treatment, cancer recurrence, and parents' experience using the internet will be collected at the eligibility interview.

Psychological and health economics outcomes
Symptoms of posttraumatic stress (PTSS) will be assessed using the revised Posttraumatic Stress Disorder Checklist for DSM-5 (PCL-5)[34] and the DSM-IV (PCL-C) [35] for comparison with our previous studies.[5, 11, 12, 18] Symptoms of depression will be assessed using the Patient Health Questionnaire (PHQ-9),[36] the GAD-7 [37] will be used to assess symptoms of anxiety. Frequency of parental fear of cancer recurrence and of their child experiencing another serious health condition will be measured by 5 item Likert scales developed by the study authors LvE, JW, and AW, and rated from "very often" to "not at all". Psychological inflexibility and experiential avoidance will be measured with the Acceptance and Action Questionnaire, 6-items (AAQ-6).[38] The Behavioural Activation for Depression Scale (BADS)[39] will be used to measure depressive inactivity. Symptoms of fatigue will be measured with the Fatigue Severity Scale (FSS),[40] and the Self-Compassion Scale-Short form (SCS-SF)[41] will be used to measure self-compassion. The EQ-5D [42] will be used to assess quality of life, with impact on use of healthcare services, employment, absence, and sick leave examined with a modified short-version of the Trimbos and Institute of Medical Technology Assessment Cost Questionnaire for Psychiatry (TiC-P),[43] assessing direct and

Table 2. Overview of feasibility outcomes and progression criteria

Outcome	Evaluation	Progression criteria to controlled trial[1]
Recruitment and eligibility	• Number identified via the Swedish Childhood Cancer Registry and the Swedish Tax Agency and/or via advertisements	No criteria set
	• Percentage assessed for eligibility; fulfilling inclusion criteria, and included (of total number identified)	≥9% interested in participating of total participant population
	• Ambiguities regarding eligibility criteria	No criteria set
	• Reasons for ineligibility	No criteria set
	• Reasons for non-participation	No criteria set
Data collection	• Percentage completing assessments	≥70% answering all questions at all assessments
	• Numbers of missing items	≤10% per questionnaire
	• Types and number of potential uncertainties in diagnostic interviews	No criteria set
Attrition	• Rates of study dropout	≤30%
	• Rate of intervention dropout	≤30%
Resources needed to complete the study and the intervention	Length of time required for: • participants to work through the intervention • participants to complete questionnaires and interviews • e-therapists to deliver the intervention • study personnel to administer the study	No criteria set
Participants' adherence to intervention	Number of: • opened introductory chapters • opened CBT modules, completed action plans • completed video or telephone assessment sessions • completed 'booster' support sessions	≥50% attending the video or telephone assessment session, completing the introductory chapter, 5 CBT modules and the 'booster' support session.
Participants use of the intervention	Number of: • logins • use of optional support functions	No criteria set
E-therapists' adherence to intervention	• Content of internet-administered written e-therapist-parent communication	No criteria set
Participants' acceptability of intervention and data	• Reasons for poor attendance and withdrawal from study and intervention	No criteria set

collection and exploration of mechanisms of impact	• Impressions and experiences of working with the intervention (including positive and negative consequences) and of completing questionnaires and interviews	≥70% of participants using the intervention reporting that it is helpful <1 participant reporting substantial negative consequences related to participation in the study and/or intervention

[1]If one or more criteria are not met revisions should be considered before proceeding to a controlled trial.

indirect medical costs and indirect non-medical costs. The M.I.N.I neuropsychiatric interview [26] will be used to assess current psychiatric disorders.

Data collection

Data will be collected via telephone and/or the Portal at the eligibility interview, baseline, post-treatment (12 weeks), and at six-month follow-up. In order to minimise attrition, prompts will be sent to indicate it is time to complete the next assessment, with parents able to indicate how they would prefer to receive prompts (e.g., via e-mail, telephone, text message or post). Additional reminders will be sent when assessments have not been completed within one week following a prompt. If parents do not complete post-treatment (12 weeks) and six-month follow-ups on the Portal within two weeks of receiving the first prompt, they will be provided with an option to complete the outcome measurements over the telephone with a member of the research team. A study newsletter will be sent to participants via e-mail approximately six weeks before post-treatment (12 weeks) and six-month follow-up, given evidence suggesting using study newsletters as a pre-notification device can improve follow-up rates.[44] Study newsletter content will change during the course of the study and will include both current study specific and wider research group news, alongside a reminder that the next assessment will be due in six weeks.

Weekly measures of PTSS (PCL-5; PCL-C), depression (PHQ-9), experiential avoidance (AAQ-6), and depressed inactivity (BADS) will be collected via the Portal during the intervention to examine the feasibility of collecting quantitative process evaluations data. All measurements collected during the course of the study, including mode of administration at each assessment, are shown in Table 3.

Participant adherence

Opened modules, completed action plans, and private messages to e-therapists will be logged via the Portal to examine adherence to the intervention. Further, total number of logins and use of optional support functions will be logged to examine use of the intervention. Full adherence to the intervention will be defined as: (1) attendance of the initial individual assessment session, via video or telephone; (2) completion of the introductory chapter; (3) completion of five CBT modules, as defined by submission of each associated action plan to the e-therapist; and (4) attendance of the 'booster' support session.

E-therapist adherence

To assess e-therapist adherence, improve training, and identify areas requiring further modification or development, all video and telephone support sessions will be recorded with parent consent and reviewed by a clinical supervisor external to the research team. In addition, e-mail communication will be reviewed by the clinical supervisor to further ensure adherence to the intervention and adequacy of e-therapist competency. Furthermore, a 15% sample of the written and 15% of video/telephone communication between e-therapists and parents will be reviewed for e-therapist adherence and competence in supporting the intervention according to an adherence measure developed for the ENGAGE intervention, performed by a member of the research team (with relevant clinical expertise), otherwise not associated with the study.

Qualitative process evaluation

Semi-structured interviews will be conducted by a psychologist with parents via the telephone at baseline and post-treatment (12 weeks). Sample size cannot be stated a priori and interviews will be conducted until data saturation is met.

Table 3. Overview of measures at the respective assessments

Variable/Phenomena	Measure	Eligibility interview	Baseline	Post-assessment	Weekly process evaluation	Six-month follow-up	Mode of administration
Child age, gender, diagnosis, date of first diagnosis, date of end of treatment (where available), and type of treatment	The Swedish Childhood Cancer Registry						Swedish Childhood Cancer Registry (Recruitment strategy A)/Telephone (Recruitment strategy B)
Inclusion and exclusion criteria; parent background data; date of end of treatment of child's treatment and whether child has had any recurrence	Structured questions	✓					Telephone
Psychiatric (mood and anxiety) disorders, drug and alcohol, misuse, and suicidality	M.I.N.I.	✓		✓		✓	Telephone
Presenting psychological difficulties and related needs; expectations concerning the ENGAGE intervention; main distressing concerns regarding healthcare utilisation and productivity losses related to their child's cancer	Semi-structured questions		✓				Telephone
PTSS	PCL-5		✓	✓	✓	✓	Portal/Telephone Only Portal during intervention
PTSS	PCL-C		✓	✓	✓	✓	Portal/Telephone Only Portal during intervention
Depression	PHQ-9		✓	✓	✓	✓	Portal/Telephone Only Portal during intervention
Anxiety	GAD-7		✓	✓		✓	Portal/Telephone

Fear of recurrence	Structured question	✓	✓		✓	Portal/Telephone
Fear of serious health condition	Structured question	✓	✓		✓	Portal/Telephone
Psychological inflexibility and experiential avoidance	AAQ-6	✓	✓	✓	✓	Portal/Telephone Only Portal during intervention
Depressed inactivity	BADS	✓	✓	✓	✓	Portal/Telephone Only Portal during intervention
Fatigue	FSS	✓	✓		✓	Portal/Telephone
Quality of life	EQ-5D	✓	✓		✓	Portal/Telephone
Self-compassion	SCS-SF	✓	✓		✓	Portal/Telephone
Health economics	TiC-P	✓	✓			Portal/Telephone
Acceptability of the intervention; e-therapist; and study procedures; views concerning the impact of the ENGAGE intervention. Non-attendees and poor-attendees are asked about reasons for disengaging, barriers to treatment, and suggestions for future intervention development and study procedures.	Semi-structured questions		✓			Telephone

Note: AAQ-6, Acceptance and Action Questionnaire; BADS, Behavioural Activation for Depression Scale; EQ-5D, EuroQol 5-dimension questionnaire; FSS, Fatigue Severity Scale; FRRS, Fear of Recurrence; GAD-7, Generalized Anxiety Disorder 7-item scale; M.I.N.I, Mini-International Neuropsychiatric Interview; PCL-5 Posttraumatic Stress Disorder Checklist for DSM-5, PCL-C Posttraumatic Stress Disorder Checklist-Civilian version; PHQ-9, Patient Health Questionnaire; SCS-SF, Self-Compassion Scale-Short form; TiC-P, Trimbos and Institute of Medical Technology Assessment Cost Questionnaire for Psychiatry.

Baseline: Participants will be asked to describe their main presenting psychological difficulties and related needs, and expectations concerning the ENGAGE intervention. To inform any future health economic evaluation, they will be asked to describe distressing concerns regarding healthcare utilisation and productivity losses related to their child's cancer disease.

Post-treatment: Parents will be interviewed to explore the acceptability of the ENGAGE intervention and associated study procedures. In order to examine possible mechanisms of change, parents' views concerning the impact of the ENGAGE intervention and CBT techniques had on their mood, and lives more generally, will be explored. The interview guide will be informed by previous research examining the acceptability of CBT self-help interventions [45-47] and qualitative process evaluations.[48] To explore the non-acceptability of the intervention, study procedures, and potential barriers to treatment, non-attendees (parents who do not attend the initial video or telephone assessment session or complete the introductory chapter or any modules) and poor-attendees (attend the initial video or telephone assessment with an e-therapist but disengage prior to completion of the introductory chapter and at least five modules alongside the attendance of the 'booster' support session), will be invited to be interviewed. Semi-structured interviews with non-attendees and poor attendees will explore reasons for disengaging, barriers to treatment, and examine suggestions for future intervention development and study procedures.

Data analyses

Data analyses will primarily be descriptive and will address the outcomes relating to the feasibility of the intervention and study procedures. Progression criteria will be used to determine whether revisions should be considered before proceeding to a controlled trial (Table 2).[22]

Quantitative analyses

An adapted CONSORT diagram for pilot and feasibility studies [23] will be used to illustrate participant flow. Numbers of parents identified via the Swedish Childhood Cancer Foundation and NAVET registry (Swedish Tax Agency) or by advertisements, numbers expressing initial interest, consented, assessed for eligibility, eligible, and included, will be reported. The percentages of: (1) parents assessed for eligibility of the total number invited; (2) parents meeting eligibility criteria of the total number invited; and (3) parents enrolled in the study of the total number invited will be calculated with exact 95% confidence intervals. Reasons for ineligibility, ambiguities regarding eligibility criteria, and reasons for non-participation will be reported at each stage.

Follow-up rates and numbers of missing items relating to outcome measures will be calculated with 95% confidence intervals. In addition, means and standard deviations for the number of reminders sent via text message, e-mail, and telephone will be reported. Potential assessment uncertainties in diagnostic interviews will be reported alongside means and standard deviations for time taken to complete questionnaires and interviews. Descriptive statistics including the means and standard deviations or medians and interquartile ranges and change scores for each outcome measurement at the eligibility interview, baseline, and post-treatment, and at six-month follow-up will be reported. Attrition proportions (both intervention and study dropout) will be reported with 95% confidence intervals.
Means, standard deviations, and frequencies for each Portal activity relating to intervention adherence and use, including logins, opened modules and items, completed action plans and use of optional support functions will be reported. Means, standard deviations, and

frequencies of parent and e-therapist contact within the Portal, via telephone and/or video will be reported and e-therapist adherence measures will be summarised with means and standard deviations and collated in total and by e-therapist.

Means and standard deviations for the length of time taken for parents to work through the intervention and for parents to complete the eligibility interview, baseline, post-treatment (12 weeks), and six months follow-up assessments will be reported. In addition, means and standard deviations will be reported for the length of time e-therapists spend delivering the intervention; for therapist training and supervision, and for project personnel to administer the data collection procedures from invitation through follow-up. This data will be used to assess the feasibility of the intervention and study procedures. Potential ambiguities regarding standard safety procedures, types and numbers of measures undertaken to assure patient safety, and types and numbers of unforeseen safety issues will be reported.

Qualitative analyses

Answers to semi-structured interview questions will be recorded, transcribed verbatim, checked for accuracy, and analysed using qualitative content analysis.[49] To increase trustworthiness of the analysis, at least two researchers and parent research partners will be involved in all stages of analysis to increase credibility, and ensure results accurately represent parents' experiences. Disconfirming case analysis [50] will be conducted to further improve rigour and trustworthiness. Content analysis [51] will be used to analyse the written communication in the interactive functions of the intervention.

ETHICS AND DISSEMINATION

The study has been approved by the Regional Ethical Review Board in Uppsala, Sweden (Dnr: 2017/527) and will be conducted in accordance to the Helsinki Declaration, ensuring the welfare and rights of all participants. Confidentiality will be guaranteed and consideration will be given to participants' integrity, dignity, and vulnerability. Informed consent will be collected to ensure participants are aware of the conditions of study participation. Participants will be reminded of their rights to withdraw from the study without giving any reason. Participants will be provided with contact information within the study invitation packs for both the principal investigator (co-author LvE) and the independent Patient Health and Safety Officer for the U-CARE group should they have any cause for concern regarding the conduct of the trial. All data will be handled according to Patient Data Act (2008:355) and the General Data Protection Regulation (EU 2016/679) with all participants assigned a study code to de-identify data and personal information about participants stored separately from de-identified data. Data collected via the Portal will be stored on secure servers at Uppsala University, with personal data and user-generated data stored on separate databases on different servers. The Portal secures de-identification of data and prevents unauthorised persons to connect data from different Portal databases. All other data will be stored in a locked filing cabinet, accessible only to study personnel. Responsible healthcare provider will be U-CARE Healthcare operating according to the Patient Safety Act (2010:659), Patient Data Act (2008:355) and the Health and Medical Services Act (2017:30). Any adverse events or negative effects discovered during the study will be reported following standard U-CARE Healthcare procedures. Assessments are carried out throughout the study to ensure participants in need of more extensive support, than provided within the study, are identified and guided to appropriate healthcare services. Communication within the Portal will be monitored to identify participants at risk of harm to self or signalling a need for more extensive support. Study findings will be published in an open access journal and via national and international conference presentations.

DISCUSSION

The ENGAGE intervention was developed in response to previous research demonstrating that a substantial subgroup of parents of children previously treated for cancer reports psychological distress in response to their child's disease [3-6] and/or an unmet need of psychological support.[9] Psychological distress related to a child's cancer disease not only cause suffering but also costs to the individual parent.[51, 52] Findings for other populations show that this kind of distress also is costly for society as a whole due to impacts on healthcare utilization and productivity loss.[53] Challenges faced by the Swedish healthcare sector concerning a widening gap between mental health treatment demands and available resources can potentially be addressed using internet-administered interventions supported by cost-effective e-therapists. We have recently published findings demonstrating the clinical effectiveness of an internet-administered psychological, self-help, intervention for parents of children recently diagnosed with cancer.[11, 12] However to the best of our knowledge there is no published evaluation of the clinical efficacy and cost-effectiveness of such an intervention for psychological distress experienced by parents of children previously treated for cancer.

The study presented in this protocol will examine the feasibility and acceptability of ENGAGE, an internet-administered, guided, CBT-based self-help intervention developed to reduce psychological distress among parents of children previously treated for cancer. Investigating the feasibility and acceptability of complex interventions and study procedures is strongly recommended to estimate important parameters and answer key uncertainties required to inform the design of future definitive controlled trials.[54] Given the novelty of the intervention, and limited number of intervention studies conducted with the target population, assessing the acceptability and feasibility of the intervention and study procedures is of great importance in informing intervention refinements and the planning of a future definitive controlled trial. Should the ENGAGE intervention and procedures be demonstrated to be feasible and acceptable, the intervention will be evaluated in a definitive controlled trial. In turn, should the intervention be demonstrated to be clinically and cost effective, the aim is to implement the intervention within the standard Swedish healthcare setting.

Study status: Recruitment is planned to commence during autumn 2018.

ACKNOWLEDGEMENTS

The authors wish to express their gratitude to everyone who has contributed to the development of the intervention and study procedures, especially to the parent and expert research partners and facilitators involved in the development.

AUTHOR CONTRIBUTIONS

Last author LvE conceived the idea for the project and secured funding. LvE and JW developed the methodology and analysis plan with contributions from MC, HG, GL, AR, and AW. LvE, MC, and AW contributed to the development of the intervention. All authors made substantial contributions to the drafting, critical revision, and final approval of the manuscript.

FUNDING STATEMENT

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COMPETING INTERESTS

None declared.

ETHICAL APPROVAL

Ethical approval was granted by the Regional Ethical Review Board in Uppsala, Sweden (Dnr: 2017/527).

SPONSORS

Professor Louise von Essen is the principal investigator and conceived the intervention and the study design and is providing on-going management of the study. The Uppsala University is acting as the study sponsor.

REFERENCES

1. Gustafsson G, Kogner P, Heyman M. Childhood cancer incidence and survival in Sweden 1984-2010. *Swedish Childhood Cancer Registry* 2013. http://www.forskasverige.se/wp-content/uploads/ChildhoodCancerIncidenceandSurvivalinSweden1984_2010.pdf (accessed 9 November 2017)
2. Pai ALH, Greenley RN, Lewandowski A, et al. A meta-analytic review of the influence of pediatric cancer on parent and family functioning. *J Fam Psychol* 2007;21(3):407-15. doi: 10.1037/0893-3200.21.3.407
3. Wakefield CE, McLoone JK, Butow P, Lenthen K, Cohn RJ. Parental adjustment to the completion of their child's cancer treatment. *Pediatr Blood Cancer* 2011;56(4):524-31. doi: 10.1002/pbc.22725
4. Ljungman L, Cernvall M, Grönqvist H, et al. Long-term positive and negative psychological late effects for parents of childhood cancer survivors: a systematic review. *PLoS One* 2014;9(7):e103340. doi: 10.1371/journal.pone.0103340
5. Ljungman L, Hovén E, Ljungman G, et al. Does time heal all wounds? A longitudinal study of the development of posttraumatic stress symptoms in parents of survivors of childhood cancer and bereaved parents. *Psychooncology* 2015;24:1792–98. doi: 10.1002/pon.3856
6. Bruce M. A systematic and conceptual review of posttraumatic stress in childhood cancer survivors and their parents. *Clin Psychol Rev* 2006;26(3):233-56. doi: 10.1016/j.cpr.2005.10.002
7. Wijnberg-Williams BJ, Kamps WA, Klip EC, et al. Psychological adjustment of parents of pediatric cancer patients revisited: five years later. *Psychooncology* 2006;15(1):1-8. doi: 10.1002/pon.927
8. Steele AC, Mullins LL, Mullins AJ, et al. Psychosocial interventions and therapeutic support as a standard of care in pediatric oncology. *Pediatr Blood Cancer* 2015;62:S585-S618. doi: https://doi.org/10.1002/pbc.25701
9. Kukkola L, Hovén E, Cernvall M, et al. Perceptions of support among Swedish parents of children after end of successful cancer treatment: a prospective, longitudinal study. *Acta Oncol* Published online First: 3 October 2017. doi: 10.1080/0284186X.2017.1374554
10. Wakefield CE, McLoone J, Butow P, et al. Support after the completion of cancer treatment: perspectives of Australian adolescents and their families. *Eur J Cancer Care* 2013;22(4):530–9. doi: 10.1111/ecc.12059
11. Cernvall M, Carlbring P, Ljungman L, et al. Internet-based guided self-help for parents of children on cancer treatment: a randomized controlled trial. *Psychooncology* 2015;24(9):1152-8. doi: 10.1002/pon.3788
12. Cernvall M, Carlbring P, Wikman A, et al. Twelve-month follow-up of a randomized controlled trial of internet-based guided self-help for parents of children on cancer treatment. *J Med Internet Res* 2017;19(7):e273. doi: 10.2196/jmir.6852
13. Stehl ML, Kazak AE, Alderfer MA, et al. Conducting a randomized clinical trial of an psychological intervention for parents/caregivers of children with cancer shortly after diagnosis. *J Pediatr Psychol* 2009;34(8):803-16. doi: 10.1093/jpepsy/jsn130
14. Knowles SE, Toms G, Sanders C, et al. Qualitative meta-synthesis of user experience of computerised therapy for depression and anxiety. *PLoS One* 2014;9(1):e84323. doi: 10.1371/journal.pone.0084323

15. Scott K, Beatty L. Feasibility study of a self-guided cognitive behaviour therapy Internet intervention for cancer carers. *Aust J Prim Health* 2013; 19(4):270-74. doi: 10.1071/PY13025
16. Ferwerda M, van Beugen S, van Burik A, et al. What patients think about E-health: patients' perspective on internet-based cognitive behavioral treatment for patients with rheumatoid arthritis and psoriasis. *Clin Rheumatol* 2013;32(6):869-73. doi: 10.1007/s10067-013-2175-9
17. Craig P, Dieppe P, Macintyre S, et al. Developing and evaluating complex interventions: the new Medical Research Council guidance. *Int J Nurs Stud* 2013;50(5):587-92. doi: 10.1016/j.ijnurstu.2012.09.010
18. Ljungman L*, Cernvall M*, Ghaderi A, et al. An open trial of individualized face-to-face cognitive behavior therapy for psychological distress in parents of children after end of treatment for childhood cancer including a cognitive behavioral conceptualization. *PeerJ*, forthcomming 2018.
19. Kindon S, Kesby M, Pain R. Participatory action research approaches and methods: connecting people, participation and place. 1st ed. New York: Routhledge; 2007.
20. Wikman A, Kukkola L, Börjesson H, et al. Development of an internet-administered cognitive behavioral therapy program (ENGAGE) for parents of children previously treated for cancer: a participatory action research approach. *JMIR,* forthcoming 2018.
21. Eldridge S, Lancaster G, Campbell M, et al. Defining feasibility and pilot studies in preparation for randomised controlled trials: development of a conceptual framework. *PLoS One* 2016;11(3):e0150205.
22. Thabane L, Ma J, Chu R, et al. A tutorial on pilot studies: the what, why and how. *BMC Med Res Methodol* 2010;10:1. doi: 10.1186/1471-2288-10-1
23. Eldridge SM, Chan CL, Campbell MJ, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. *BMJ* 2016;355:i5239. doi: 10.1136/bmj.i5239
24. Moore GF, Audrey S, Barker M, et al. Process evaluation of complex interventions: Medical Research Council guidance. *BMJ* 2015;350:h1258. doi: 10.1136/bmj.h1258.
25. Chan A-W, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. *Ann Intern Med* 2013;158(3):200-7.
26. Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry* 1998;59 (Suppl 20):22-33.
27. Sim J, Lewis M. The size of a pilot study for a clinical trial should be calculated in relation to considerations of precision and efficiency. *J Clin Epidemiol* 2012;65(3):301-8. doi: 10.1016/j.jclinepi.2011.07.011
28. Bower P, Brueton V, Gamble C, et al. Interventions to improve recruitment and retention in clinical trials: a survey and workshop to assess current practice and future priorities. *Trials* 2014;15:399. doi: 10.1186/1745-6215-15-399
29. Barnes M, Wiles N, Morrison J, et al. Exploring patients' reasons for declining contact in a cognitive behavioural therapy randomised controlled trial in primary care. *Br J Gen Pract* 2012;62(598):e371-7. doi: 10.3399/bjgp12X641492
30. Farrand P, Woodford J, Llewellyn D, et al. Behavioural activation written self-help to improve mood, wellbeing and quality of life in people with dementia supported by informal carers (PROMOTE): a study protocol for a single-arm feasibility study. *Pilot Feasibility Stud* 2016;2:42. doi: 10.1186/s40814-016-0083-x
31. Ridgway N, Williams C. Cognitive behavioural therapy self-help for depression: an overview. *J Ment Health* 2011;20:593–603. doi: 10.3109/09638237.2011.613956

32. Farrand P, Woodford J. Impact of support on the effectiveness of written cognitive behavioural self-help: a systematic review and meta-analysis of randomised controlled trials. *Clin Psychol Rev* 2013;33(1):182-95. doi: 10.1016/j.cpr.2012.11.001
33. Barazzone N, Cavanagh K, Richards DA. Computerized cognitive behavioural therapy and the therapeutic alliance: a qualitative enquiry. *Br J Clin Psychol* 2012;51(4):396-417. doi: 10.1111/j.2044-8260.2012.02035.x
34. Weathers FW, Litz BT, Keane TM, et al. The PTSD Checklist for DSM-5 (PCL-5). *National Center for PTSD* 2013. www.ptsd.va.gov (accessed 10 November 2017)
35. Weathers FW, Litz BT, Herman DS, et al. The PTSD Checklist (PCL):reliability, validity, and diagnostic utility. Paper presented at the 9th Annual Conference of the ISTSS. San Antonio (TX); 1993.
36. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001;16(9):606-13.
37. Spitzer RL, Kroenke K, Williams JB, et al. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med* 2006;166(10):1092-7. doi: 10.1001/archinte.166.10.1092
38. Lundgren T, Parling T. Swedish Acceptance and Action Questionnaire (SAAQ): a psychometric evaluation. *Cogn Behav Ther* 2017;46(4):315-26. doi: 10.1080/16506073.2016.1250228
39. Kanter JW, Mulick PS, Busch AM, et al. The Behavioral Activation for Depression Scale (BADS): psychometric properties and factor structure. *J Psychopathol Behav Assess* 2007;29:191-202. doi: 10.1007/s10862-006-9038-5
40. Krupp LB, LaRocca NG, Muir-Nash J, et al. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. *Arch Neurol* 1989;46(10):1121-3.
41. Raes F, Pommier E, Neff KD, et al. Construction and factorial validation of a short form of the Self-Compassion Scale. *Clin Psychol Psychother* 2011;18(3):250-5. doi: 10.1002/cpp.702
42. EuroQol Group. EuroQol--a new facility for the measurement of health-related quality of life. *Health Policy* 1990;16(3):199-208.
43. Bouwmans C, De Jong K, Timman R, et al. Feasibility, reliability and validity of a questionnaire on healthcare consumption and productivity loss in patients with a psychiatric disorder (TiC-P). *BMC Health Serv Res* 2013;13:217. doi: 10.1186/1472-6963-13-217
44. Mitchell N, Hewitt CE, Lenaghan E, et al. Prior notification of trial participants by newsletter increased response rates: a randomized controlled trial. *J Clin Epidemiol* 2012;65(12):1348-52. doi: 10.1016/j.jclinepi.2012.05.008
45. Hind D, O'Cathain A, Cooper CL, et al. The acceptability of computerised cognitive behavioural therapy for the treatment of depression in people with chronic physical disease: a qualitative study of people with multiple sclerosis. *Psychol Health* 2010;25(6):699-712. doi: 10.1080/08870440902842739
46. Farrand P, Woodford J, Small F, et al. Behavioural activation self-help to improve depression in people living with dementia: The PROMOTE treatment protocol. *NZ J Psychol* 2017;46(2):51-62. doi: 10.1186/s40814-016-0083-x
47. Ander M, Wikman A, Ljótsson B, et al. Guided internet-administered self-help to reduce symptoms of anxiety and depression among adolescents and young adults diagnosed with cancer during adolescence (U-CARE: YoungCan): study protocol for a feasibility trial. *BMJ Open* 2017;7(1):e013906. doi: 10.1136/bmjopen-2016-013906

48. Finning K, Richards DA, Moore L, et al. Cost and outcome of behavioural activation versus cognitive behavioural therapy for depression (COBRA): a qualitative process evaluation. *BMJ Open* 2017;**7**(4):e014161. doi: 10.1136/bmjopen-2016-014161
49. Graneheim UH, Lundman B. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. *Nurse Educ Today* 2004;24(2):105-12. doi: 10.1016/j.nedt.2003.10.001
50. Patton MQ. Qualitative evaluation and research methods. 2nd ed. Newbury Park (CA): Sage; 1990.
51. Mader L, Roser K, Baenziger J, et al. Household income and risk-of-poverty of parents of long-term childhood cancer survivors. *Pediatr Blood Cancer* 2017;64(8). doi: 10.1002/pbc.26456
52. Lindahl Norberg A, Montgomery SM, Bottai M, et al. Short-term and long-term effects of childhood cancer on income from employment and employment status: a national cohort study in Sweden. *Cancer*, 2017;123(7):1238-48. doi: 10.1002/cncr.30436
53. Smit F, Cuijpers P, Oostenbrink J, et al. Costs of nine common mental disorders: implications for curative and preventive psychiatry. *J Ment Health Policy Econ* 2006;9(4):193-200.
54. Eldridge SM, Lancaster GA, Campbell MJ, et al. Defining feasibility and pilot studies in preparation for randomised controlled trials: development of a conceptual framework. *PLoS One* 2016;11(3):e0150205. doi: 10.1371/journal.pone.0

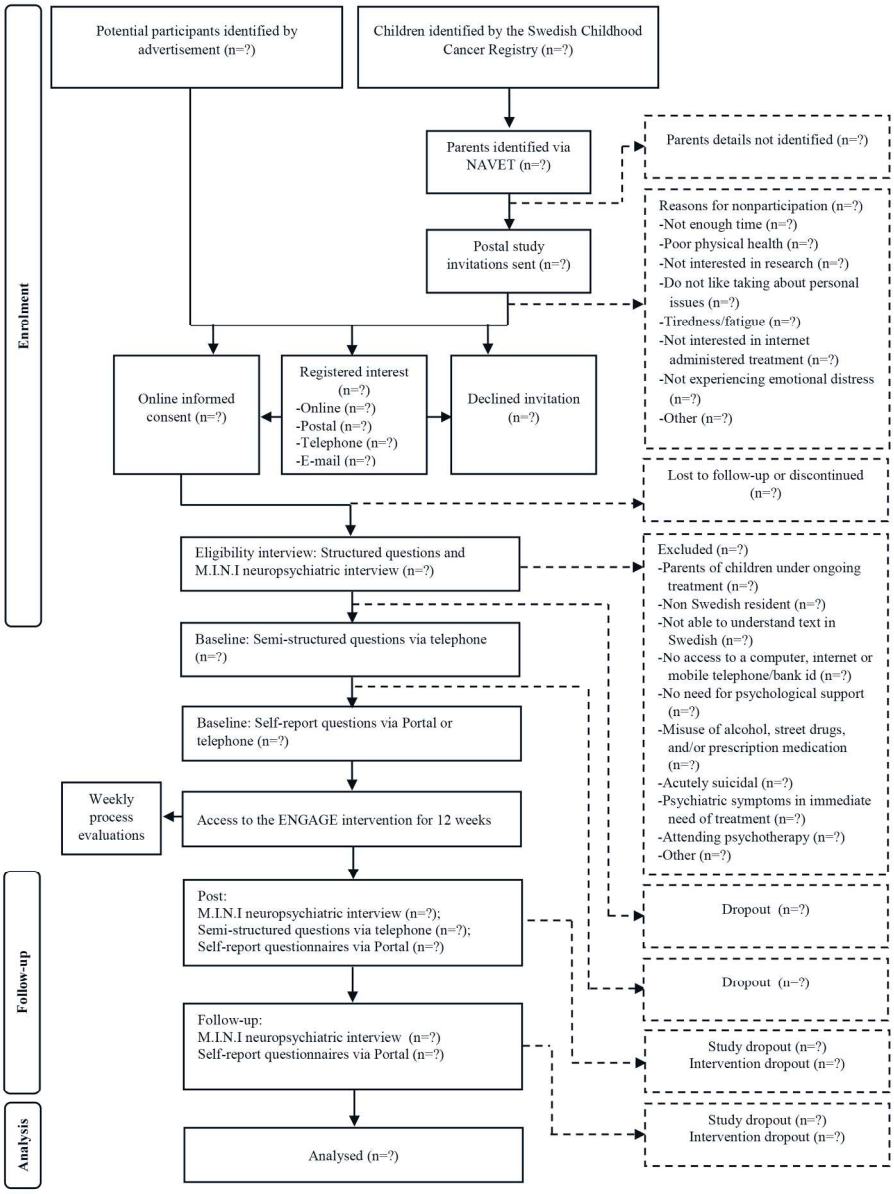

Figure 1. CONSORT-diagram

176x232mm (300 x 300 DPI)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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		Reporting Item	Page Number
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	Throughout
Protocol version	#3	Date and version identifier	5
Funding	#4	Sources and types of financial, material, and other support	19
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1, 18
Roles and	#5b	Name and contact information for the trial sponsor	19

responsibilities: sponsor contact information			
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	19
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N.A
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	N.A
Objectives	#7	Specific objectives or hypotheses	5
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	5
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	10
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	5, 7, 9

Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7-10 Table 1 (8)
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	N.A
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	13
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	5
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	10-15 Table 2 (11-12) Table 3 (14-15)
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	6-7 Figure 1
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	5-6
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	6
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned	N.A

		restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	N.A
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	N.A
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	N.A
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N.A
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	10-16 Figure 1 Table 2 (11-12) Table 3 (14-15)
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	6, 13, 16
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	17

Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	16-17
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	N.A
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	N.A
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	N.A
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N.A
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	N.A
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N.A
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	1, 17, 19
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	N.A

Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	6, 7, 17
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N.A
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	17
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	19
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	N.A
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N.A
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	17
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	N.A
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	N.A
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	N.A
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future	N.A

use in ancillary studies, if applicable

BMJ Open

Study protocol for a feasibility study of an internet-administered, guided, CBT-based, self-help intervention (ENGAGE) for parents of children previously treated for cancer

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Study protocol for a feasibility study of an internet-administered, guided, CBT-based, self-help intervention (ENGAGE) for parents of children previously treated for cancer

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ABSTRACT

Introduction: A subgroup of parents of children previously treated for cancer report long-term psychological distress after end of treatment. However, needs for psychological support are commonly unmet and there is a lack of evidence-based treatments tailored to the specific needs of this population. An internet-administered, guided, cognitive-behavioural therapy (CBT) based, self-help intervention (ENGAGE) for parents of children previously treated for cancer, may provide a solution. The aim is to examine the feasibility and acceptability of the intervention ENGAGE and the study procedures for a future controlled trial.

Methods and analysis: The study has an uncontrolled within group, design with an embedded qualitative and quantitative process evaluation. Potential participants are parents of children previously treated for cancer, living in Sweden, recruited via their child's personal identification number (via the Swedish Childhood Cancer Registry and the Swedish Tax Agency). Parents are invited randomly with information packs sent to home addresses. Further interest in participating can be registered via information on relevant websites. The study aims to recruit 50 parents who will receive the intervention ENGAGE which is designed to be delivered over a 10-week period, and comprises one introductory chapter followed by up to 10 intervention modules addressing key concerns identified for the population. Consistent with feasibility study objectives, primary outcomes relate to recruitment, attrition, data collection, study resources, intervention delivery and acceptability. Clinical outcomes (posttraumatic stress, depression, anxiety, fear of cancer recurrence, psychological inflexibility and experiential avoidance, depressed inactivity, fatigue, quality of life, and self-compassion) will be measured at baseline-, post-treatment (12 weeks), and six-month follow-up.

Ethics and dissemination: The Regional Ethical Review Board in Uppsala, Sweden has granted approval for the study (Dnr: 2017/527). Results will be disseminated to relevant healthcare and patient communities, in peer-reviewed and popular science journals, and at scientific and clinical conferences.

Keywords: Parents; eHealth; Depression; Anxiety; Clinical trial

Trial registration number: ISRCTN57233429

ARTICLE SUMMARY

Strengths and limitations of this study

- Development of the internet-administered, guided, CBT based, self-help intervention ENGAGE has included not only consulting of theoretical literature and clinical expertise but also extensive involvement of end-users by means of Participatory Action Research.
- This study will examine the feasibility and acceptability of the intervention ENGAGE alongside planned study procedures for a controlled trial.
- This study will examine methodological, procedural, and clinical challenges to revise and refine the intervention ENGAGE, study design, and planned procedures prior to a controlled trial following established feasibility study progression criteria.
- This study is limited to examining the feasibility and acceptability of intervention delivery within a university setting and does not examine the feasibility of implementation within a real-life healthcare context.

INTRODUCTION

Most children diagnosed with cancer survive their disease.[1] However, childhood cancer impacts on the whole family from diagnosis into survivorship.[2] For parents, a child's treatment completion is not only an important milestone but also a period of psychological vulnerability.[3, 4] A subgroup report negative long-term psychological consequences years after treatment completion.[4-7] However, there is a lack of evidence-based psychological interventions for parents who experience distress in relation to a child's cancer disease after end of treatment. Recently published guidelines, informing how children diagnosed with cancer and their family members should be cared for, recommend referrals to appropriate therapeutic support into long-term survivorship.[8] However, significant challenges remain regarding provision of such support. We have reported an unmet need of psychological support among parents of children previously treated for cancer.[9] The results are in line with findings from an Australian study showing that formal psychological support was difficult to access and rarely received by parents after completion of cancer treatment.[10] Factors related to staff availability, models of assessment and delivery of services, and size and location of paediatric cancer units hindered provision of support.

Using the internet to deliver psychological support may increase access to support and represent an alternative model of psychological support delivery for parents of children previously treated for cancer. We have shown an internet-administered psychological, self-help intervention to be effective in reducing symptoms of anxiety, depression, and posttraumatic stress (PTSS) among parents of children recently diagnosed with cancer,[11] with improvements maintained at one year follow-up.[12] However, challenges with recruitment and attrition were encountered, indicating that end-user involvement in the development of interventions, alongside informing study procedures to test and evaluate interventions, may be essential for intervention research within this population.[13] Research suggests internet-administered, self-help interventions should be developed with the target population in mind,[14] with lower levels of acceptability found for internet-administered interventions not developed for a specific population.[15] Additionally, recruitment and adherence rates may improve if the perspective of the population is adopted.[16] Finally, there is currently a lack of evidence-based psychological support for parents who experience distress in relation to a child's cancer disease after successful cancer treatment, despite clear findings showing that a subgroup of parents report long-term psychological distress.[4, 5, 9]

The aim is to examine the feasibility and acceptability of the internet-administered, CBT-based, guided, self-help intervention ENGAGE for parents of children previously treated for cancer and the study procedures for a future controlled trial. We have undertaken a programme of Phase I (development) research, following the Medical Research Council (MRC) complex interventions framework [17] to inform the development of the intervention. First, a systematic review of cancer-related long-term negative and positive psychological effects for parents of childhood cancer survivors was conducted,[4] with results used to inform the development and piloting of a face-to-face CBT based intervention. The intervention was successful, resulting in improvements in symptoms of anxiety, depression, and PTSS (d=0.65-0.92) at post-treatment and three-month follow-up.[18] Subsequently a Participatory Action Research (PAR)[19] approach was adopted to inform the design, content, and delivery of the intervention in collaboration with parent and expert research partners.[20] Finally, an online survey study, utilizing a population-based cross-sectional design, further examined preferences regarding study procedures e.g. type of controlled design and mode of recruitment (letter versus postal card).["Personal communication" by J Woodford, 20180406] Parents of children who had completed cancer treatment were invited to complete the survey,

with 32% (n=112) of 350 responding. Findings indicated no differences in response rate between mode of invitation (n=59 [34%] letter, n=53 [30%] postal card; p=0.447). Overall, parents perceived proposed study procedures (e.g., receipt of initial study information via postal letter, presentation of detailed study information online, via text and informational video, randomisation) and the receipt of internet-administered psychological support as acceptable. These findings informed the recruitment and provision of study information procedures to be further examined in the present feasibility study.

The key feasibility outcomes examined via the proposed protocol concern methodological, procedural, and clinical uncertainties,[21-23] including: (1) estimates of likely recruitment and retention rates; (2) feasibility and acceptability of data collection instruments and data collection procedures; and (3) feasibility and acceptability of the intervention. In line with standard feasibility study objectives [21] improvements regarding clinical outcomes are not examined at this stage. However, an embedded qualitative process evaluation [24] will be used to examine the: (1) acceptability of intervention; (2) self-reported psychological needs; (3) parents' healthcare utilization and productivity losses related to the child's cancer disease; (4) potential mechanisms of change; and (5) the impact of the intervention on parents' difficulties.

METHODS AND ANALYSIS

This protocol (version 1, 14/03/2018) is reported according to guidelines presented in the CONSORT 2010 statement extension for randomized pilot and feasibility studies [23] and clinical trial protocols [25].

Design

The study has an uncontrolled, within-group, baseline-, post-treatment (12 weeks), and six-month follow-up design with an embedded qualitative and quantitative process evaluation. All participants will receive the internet-administered, CBT based, self-help intervention ENGAGE, guided by an e-therapist for 10 weeks, comprising one introductory chapter followed by up to 10 treatment modules addressing key concerns identified for the population.

Eligibility criteria

Parents/caregivers (from here referred to as parents or participants) will be included according to: (1) parent of a child diagnosed with cancer when 0-18 years who has completed cancer treatment three months to five years previously; (2) resides in Sweden; (3) able to read and understand text in Swedish; (4) has access to e-mail, the internet, and a mobile telephone and/or Bank ID (a citizen authentication system used in Sweden); and (5) self-reports a need for psychological support related to the child's cancer disease and treatment. The following exclusion criteria will be used: (1) self-reported or clinician assessed (based on the M.I.N.I neuropsychiatric interview);[26] symptoms of a severe and enduring mental health difficulty; (2) self-reported or clinician assessed (based on the M.I.N.I neuropsychiatric interview);[26] misuse of alcohol, street drugs, and/or prescription medication; (3) acutely suicidal; and (4) currently attending psychological treatment. Those excluded due to a severe and enduring mental health difficulty, substance misuse, and/or acute suicidality will be guided to appropriate healthcare services.

Sample size

The eligible population includes approximately 2400 parents, with around 30% (720/2400) expected to experience a need of psychological support.[9] Approximately 30% of these (216/720) are expected to potentially consent.[11, 12, 18] Following recommendations of

sample sizes of 50-60 being appropriate to assess feasibility outcomes and estimate sample size for a definite trial [27] we aim to recruit a sample of 50 participants. If 50 are included, we will be able to estimate a participation rate of 90% within a 95% confidence interval of +/- 8%.

Recruitment

Participants will be recruited using two approaches: (A) Children's personal identification numbers will be obtained from the Swedish Childhood Cancer Registry (National Quality Registry, initiated in 1982) and linked to parents' names and addresses via NAVET, a registry held by the Swedish Tax Agency. Parents will be invited to participate randomly by the research team, using blocks of 100 until the target number of 50 has been reached. Prior to inviting parents into the study, the most up to date information concerning whether children are currently living or deceased will be checked via the telephone by a member of the research team with Swedish Tax Agency. A study information pack will be sent to home addresses, including brief information about the study and a www-address to a secure website, the U-CARE-portal (Portal). Potential participants will be able to access information via the Portal, with study information presented in text and video format. They will be able to either register interest in the study, or opt out of the study, by: (1) completing an online form via the Portal; (2) returning a reply slip using a freepost envelope; (3) telephoning the research team; or (4) e-mailing the research team. Given the use of reminders improves recruitment rates,[28] telephone numbers of those who do not respond to the research team, within four weeks of sending the postal study information pack, will be identified via internet search engines. A member of the research team will telephone all non-responders. The purpose will be to confirm receipt of the study invitation pack and answer any questions the parent may have regarding the study. In cases whereby the telephone call is not answered a maximum of four additional telephone call attempts to establish contact will be made over the following four weeks. The study information sheet will clearly specify that a member of the research team will attempt to telephone call non-responders, with parents provided with the aforementioned methods of opting out of the study should they not wish to receive a telephone call from a member of the research team. In cases whereby a participant's telephone number cannot be identified, a study information pack will be resent via the post with a reminder note added to the pack by the research team if no response is received within four weeks. (B) To raise awareness of the study, and potentially recruit to the study, advertisements will be placed on relevant social media sites and patient organizations' and interest groups' websites. People can receive more information about the study by telephoning or e-mailing the research team and register interest in the study by completing an online form via the Portal.

Reasons for non-participation

Parents deciding to opt out of further contact will be presented a short questionnaire (provided in paper format in information packs as well as online) listing possible reasons for non-participation as informed by previous research [29, 30] alongside an open-ended question for parents to provide further information and reasons for non-participation should they wish. Reasons for non-participation will be used to inform about barriers to recruitment and may provide data pertaining to the acceptability of the intervention and support offered. It will be made clear on both the paper and online questionnaire that the provision of reasons for non-participation is optional and parents do not need to report why they do not wish to participate if they would prefer not to.

Informed consent, screening, and baseline

Parents interested in participating will be asked to provide informed consent and contact

details via the Portal. Those who reply to the research team via a postal reply slip, telephone, or e-mail, will be called by a member of the research team, who will provide more information about the study. Those interested in participating will be asked to provide consent via the Portal. Parents who speak to a member of the research team and express interest in the study, but do not provide online consent within two weeks, will receive a telephone follow-up call and/or e-mail from a member of the research team. Where telephone calls are not answered, a maximum of five telephone calls will be made over a period of two weeks.

Parents providing informed consent will be contacted via telephone by a licensed psychologist for an eligibility interview with the purpose of confirming inclusion and exclusion criteria. If eligibility is confirmed, parents will be instructed to complete a baseline assessment via the Portal, with the option provided to complete the assessment via the telephone if preferred. In addition, a semi-structured interview will be completed at baseline over the telephone to gain a more detailed understanding e.g. concerning presenting problems and expectations for treatment. After the full baseline assessment is completed, parents will be provided access to the ENGAGE intervention via the Portal and will be allocated to an e-therapist. Participant flow through the study is illustrated in Figure 1.

Intervention

Content

Based on standard definitions of self-help [31] and taxonomies categorising levels of support, [32] ENGAGE can be described as an internet-administered, guided, CBT based, self-help intervention. ENGAGE includes written, audio, and video materials provided online via the Portal. The intervention includes (1) a short introductory chapter, followed by 10 CBT-based modules, with a brief overview of module content shown in Table 1; (2) an initial assessment session with an e-therapist via a video or telephone call during which the individual's problems and idiographic goals are formulated and parents are directed to the short introductory chapter and first module; and (3) weekly guidance from an e-therapist via the Portal (online written feedback). The intervention is designed to be delivered over a 10 weeks period, with parents encouraged to complete one module per week. However, the intervention will be accessible to parents for a 12 weeks period to provide flexibility regarding module completion and provision of e-therapist feedback and support. Module content is based on CBT techniques and is tailored towards key concerns and difficulties experienced by parents of children previously treated for cancer as informed by previous research.[3-5, 18] Each module includes psychoeducation alongside text, audio, and video material instructing parents in the use of specific CBT based techniques. Parents will be encouraged to complete weekly action plans and symptom questionnaires for each module which will be reviewed by the e-therapist. Further, modules include case vignettes, serving to clarify important treatment principles and help parents make connections between the material and their own experiences. Extensive efforts have been made to include 'common factors' within the intervention in order to establish, develop, and maintain a therapeutic alliance.[33] As such, the intervention has been developed to engage parents in materials by including statements of empathy, genuineness, and warmth, narratives referring to struggle and recovery, examples to help parents relate the text material to their own lives, and personal metaphors for emotional distress.[33]

Guidance from e-therapists

An e-therapist will guide the use of the intervention, following a structured support protocol developed specifically for the intervention. Guidance will consist of one video or telephone

assessment session, weekly online written support, and a mid-treatment video or telephone 'booster' session. Prior to the start of the intervention parents will be contacted by an

Table 1. Overview of the 10 modules included in the ENGAGE intervention.

	Title and description	Cognitive behavioural therapy strategies
Module 1	*"What have I experienced and where am I heading?"* *Processing and normalising the cancer experience and cancer-related distress, goal setting.*	Psychoeducation about typical reactions among parents of children previously treated for cancer. Setting intervention goals and long-term goals. Identifying challenging situations.
Module 2	*"Who takes care of me?"* *Analysing current problems using functional analysis. Principles of self-compassion.*	Introducing functional analysis. Psychoeducation about self-compassion and difficult life-events. Practicing self-compassion and functional analysis.
Module 3	*"Am I really here?"* *Mindfulness and acceptance-based strategies.*	Psychoeducation about emotions and mindfulness. Practicing noticing emotions and bodily sensations. Mindfulness and acceptance-based exercises and continue practicing functional analyses.
Module 4	*"Painful experiences"* *Exposure to painful memories and emotions and introducing skills to handle challenging situations and experiences.*	Psychoeducation about painful memories and emotions, and coping with fear of recurrence. Rationale for exposure techniques. Cognitive strategies for disengaging from patterns of unhelpful thinking. Continue practicing mindfulness and functional analyses.
Module 5	*"Looking inwards"* *Managing emotional avoidance through exposure.*	Intensifying exposure with specific focus on emotional avoidance through functional analyses and further exposure techniques. Continue practicing mindfulness.
Module 6	*"The worst I've ever experienced"* *Deepened focus on painful memories and emotions through expressive writing.*	Continued psychoeducation about painful memories and emotions. Reflecting on exposure exercises, reviewing goals from start of the programme. Continue practicing mindfulness. Expressive writing task.
Module 7	*"Back to life"* *Dealing with avoidance and painful emotions through behaviour activation and functional analyses.*	Reviewing goals and identifying challenging situations that remain, plan of action. Rationale for behavioural activation. Continuing exposure exercises.
Module 8	*"Be kind to yourself"* *Skills to better take care of oneself through principles of self-compassion and*	Continued psychoeducation about behaviour activation and self-compassion. Continue to practising self-compassion and behavioural activation.

	acceptance.	
Module 9	*"Becoming your own therapist"* *Applying new skills flexibly in everyday life.*	Psychoeducation about becoming one's own therapist. Identifying challenging situations that remain, review goals and form action plans. Focus on applying new skills in everyday life in a flexible manner.
Module 10	*"Where have I been and where am I heading now?"* *Progress review and skills for maintaining progress and set-backs.*	Reviewing the intervention, what worked better/worse, skills for maintaining change and handling set-backs.

e-therapist for the individual assessment session via video-call, lasting approximately 45 minutes. For parents not wanting to participate in a video-call there is also an option to complete the call via telephone. Parents will be able to communicate their current difficulties and the e-therapist will conduct an individually tailored behaviour analysis of the parent's main difficulties, collaboratively formulate idiographic treatment goals and introduce the intervention. Although parents will work independently with the intervention, e-therapists will provide weekly, and at-need, written support messages online via the Portal throughout the intervention. E-therapist guidance will include the provision of feedback on action plans, reinforcement of progress made, validating any difficulties experienced and providing assistance problem solving difficulties. E-therapists will provide encouragement, motivation, and guidance throughout the intervention, with parents able to contact their allocated e-therapist for additional guidance, via the Portal or telephone, should they experience a need. E-therapists will be obliged to respond to parents within one working day. Given the explorative nature of the study, no maximum time limit for support has been set, though based on previous experience [11, 12] we anticipate e-therapists will spend approximately 20-30 minutes per parent each week.

Parents will be provided a 'booster' session lasting 30-45 minutes, via video or telephone call, midway through the intervention. This session will be an opportunity to further assess any potential difficulties experienced with the ongoing work, provide additional guidance and assistance problem solving, alongside the provision of encouragement and motivation. Parents who do not log in, or show low activity in the intervention, will be contacted via text message, e-mail, and/or telephone, whichever is preferred by the parent and e-therapist.

E-therapists

E-therapists will be psychology programme students, in at least their 4th year of study, having completed a minimum of their first term of advanced studies in CBT, but will have not yet begun their prescribed practical service [i.e., praktisk tjänstgöring för psykologer/PTP]. Prior to study start, all e-therapists will participate in a one-day workshop to familiarise themselves with the treatment manual and support protocol, delivered by a licenced clinical psychologist. E-therapists will receive weekly group clinical supervision sessions focussing on case discussions, skills development, and at-need supervision by a licenced clinical psychologist with relevant experience of the population.

Optional support functions
Optional support functions within the Portal will include an online library containing information about CBT, self-help, literature suggestions, links to relevant websites as well as CBT exercises from the intervention. These materials will be available as downloadable text and audio files. In addition, all exercises used in the intervention will be accessible within the library for parents to revisit. As these functions are optional and not part of the treatment, parents will not receive any recommendations from their e-therapist regarding optimal level of engagement with these support functions.

Setting
Parents will receive guidance from e-therapists located at Uppsala University, Sweden. Due to the nature of the ENGAGE intervention being online, parents are anticipated to engage with the intervention in their own homes.

Outcome measures
Feasibility outcomes
Feasibility outcomes of interest relate to methodological, procedural, and clinical uncertainties [21-23] and examine recruitment rates, eligibility criteria, data collection, attrition, resources needed to complete the study and intervention, parents' adherence to the intervention, e-therapists' adherence to the support protocol and parents' acceptability of the intervention and study procedures. Feasibility outcomes assessed are shown in Table 2 alongside the associated progression criteria (where applicable). Progression criteria have been set to facilitate the interpretation of results and to inform whether to proceed to a definite trial after the feasibility study.

Sociodemographic and clinical variables
Data on child age, gender, diagnosis, date of first diagnosis, date of end of treatment (where available), and type of treatment will be obtained from the Swedish Childhood Cancer Registry. Self-report data on parent age, gender, education, employment status, ethnicity, relationship status, number of children, ages of children, current housing situation, previous psychological treatment, previous traumatic events, physical health, date of end of child's cancer treatment, cancer recurrence, and parents' experience using the internet will be collected at the eligibility interview.

Psychological and health economics outcomes
Symptoms of posttraumatic stress (PTSS) will be assessed using the revised Posttraumatic Stress Disorder Checklist for DSM-5 (PCL-5)[34] and the DSM-IV (PCL-C) [35] for comparison with our previous studies.[5, 11, 12, 18] Symptoms of depression will be assessed using the Patient Health Questionnaire (PHQ-9),[36] the GAD-7 [37] will be used to assess symptoms of anxiety. Frequency of parental fear of cancer recurrence and of their child experiencing another serious health condition will be measured by 5 item Likert scales developed by the study authors LvE, JW, and AW, and rated from "very often" to "not at all". Psychological inflexibility and experiential avoidance will be measured with the Acceptance and Action Questionnaire, 6-items (AAQ-6).[38] The Behavioural Activation for Depression Scale (BADS)[39] will be used to measure depressive inactivity. Symptoms of fatigue will be measured with the Fatigue Severity Scale (FSS),[40] and the Self-Compassion Scale-Short form (SCS-SF)[41] will be used to measure self-compassion. The EQ-5D [42] will be used to assess quality of life, with impact on use of healthcare services, employment, absence, and sick leave examined with a modified short-version of the Trimbos and Institute of Medical Technology Assessment Cost Questionnaire for Psychiatry (TiC-P),[43] assessing direct and

Table 2. Overview of feasibility outcomes and progression criteria

Outcome	Evaluation	Progression criteria to controlled trial[1]
Recruitment and eligibility	• Number identified via the Swedish Childhood Cancer Registry and the Swedish Tax Agency and/or via advertisements	No criteria set
	• Percentage assessed for eligibility; fulfilling inclusion criteria, and included (of total number identified)	≥9% interested in participating of total participant population
	• Ambiguities regarding eligibility criteria	No criteria set
	• Reasons for ineligibility	No criteria set
	• Reasons for non-participation	No criteria set
Data collection	• Percentage completing assessments	≥70% answering all questions at all assessments
	• Numbers of missing items	≤10% per questionnaire
	• Types and number of potential uncertainties in diagnostic interviews	No criteria set
Attrition	• Rates of study dropout	≤30%
	• Rate of intervention dropout	≤30%
Resources needed to complete the study and the intervention	Length of time required for: • participants to work through the intervention • participants to complete questionnaires and interviews • e-therapists to deliver the intervention • study personnel to administer the study	No criteria set
Participants' adherence to intervention	Number of: • opened introductory chapters • opened CBT modules, completed action plans • completed video or telephone assessment sessions • completed 'booster' support sessions	≥50% attending the video or telephone assessment session, completing the introductory chapter, 5 CBT modules and the 'booster' support session.
Participants use of the intervention	Number of: • logins • use of optional support functions	No criteria set
E-therapists' adherence to intervention	• Content of internet-administered written e-therapist-parent communication	No criteria set
Participants' acceptability of intervention and data	• Reasons for poor attendance and withdrawal from study and intervention	No criteria set

collection and exploration of mechanisms of impact	• Impressions and experiences of working with the intervention (including positive and negative consequences) and of completing questionnaires and interviews	≥70% of participants using the intervention reporting that it is helpful <1 participant reporting substantial negative consequences related to participation in the study and/or intervention

[1]If one or more criteria are not met revisions should be considered before proceeding to a controlled trial.

indirect medical costs and indirect non-medical costs. The M.I.N.I neuropsychiatric interview [26] will be used to assess current psychiatric disorders.

Data collection

Data will be collected via telephone and/or the Portal at the eligibility interview, baseline, post-treatment (12 weeks), and at six-month follow-up. In order to minimise attrition, prompts will be sent to indicate it is time to complete the next assessment, with parents able to indicate how they would prefer to receive prompts (e.g., via e-mail, telephone, text message or post). Additional reminders will be sent when assessments have not been completed within one week following a prompt. If parents do not complete post-treatment (12 weeks) and six-month follow-ups on the Portal within two weeks of receiving the first prompt, they will be provided with an option to complete the outcome measurements over the telephone with a member of the research team. A study newsletter will be sent to participants via e-mail approximately six weeks before post-treatment (12 weeks) and six-month follow-up, given evidence suggesting using study newsletters as a pre-notification device can improve follow-up rates.[44] Study newsletter content will change during the course of the study and will include both current study specific and wider research group news, alongside a reminder that the next assessment will be due in six weeks.

Weekly measures of PTSS (PCL-5; PCL-C), depression (PHQ-9), experiential avoidance (AAQ-6), and depressed inactivity (BADS) will be collected via the Portal during the intervention to examine the feasibility of collecting quantitative process evaluations data. All measurements collected during the course of the study, including mode of administration at each assessment, are shown in Table 3.

Participant adherence

Opened modules, completed action plans, and private messages to e-therapists will be logged via the Portal to examine adherence to the intervention. Further, total number of logins and use of optional support functions will be logged to examine use of the intervention. Full adherence to the intervention will be defined as: (1) attendance of the initial individual assessment session, via video or telephone; (2) completion of the introductory chapter; (3) completion of five CBT modules, as defined by submission of each associated action plan to the e-therapist; and (4) attendance of the 'booster' support session.

E-therapist adherence

To assess e-therapist adherence, improve training, and identify areas requiring further modification or development, all video and telephone support sessions will be recorded with parent consent and reviewed by a clinical supervisor external to the research team. In addition, e-mail communication will be reviewed by the clinical supervisor to further ensure adherence to the intervention and adequacy of e-therapist competency. Furthermore, a 15% sample of the written and 15% of video/telephone communication between e-therapists and parents will be reviewed for e-therapist adherence and competence in supporting the intervention according to an adherence measure developed for the ENGAGE intervention, performed by a member of the research team (with relevant clinical expertise), otherwise not associated with the study.

Qualitative process evaluation

Semi-structured interviews will be conducted by a psychologist with parents via the telephone at baseline and post-treatment (12 weeks). Sample size cannot be stated a priori and interviews will be conducted until data saturation is met.

Table 3. Overview of measures at the respective assessments

Variable/Phenomena	Measure	Eligibility interview	Baseline	Post-assessment	Weekly process evaluation	Six-month follow-up	Mode of administration
Child age, gender, diagnosis, date of first diagnosis, date of end of treatment (where available), and type of treatment	The Swedish Childhood Cancer Registry						Swedish Childhood Cancer Registry (Recruitment strategy A)/Telephone (Recruitment strategy B)
Inclusion and exclusion criteria; parent background data; date of end of treatment of child's treatment and whether child has had any recurrence	Structured questions	✓					Telephone
Psychiatric (mood and anxiety) disorders, drug and alcohol, misuse, and suicidality	M.I.N.I.	✓		✓		✓	Telephone
Presenting psychological difficulties and related needs; expectations concerning the ENGAGE intervention; main distressing concerns regarding healthcare utilisation and productivity losses related to their child's cancer	Semi-structured questions		✓				Telephone
PTSS	PCL-5		✓	✓	✓	✓	Portal/Telephone Only Portal during intervention
PTSS	PCL-C		✓	✓	✓	✓	Portal/Telephone Only Portal during intervention
Depression	PHQ-9		✓	✓	✓	✓	Portal/Telephone Only Portal during intervention
Anxiety	GAD-7		✓	✓		✓	Portal/Telephone

Fear of recurrence	Structured question	✓	✓		✓	Portal/Telephone
Fear of serious health condition	Structured question	✓	✓		✓	Portal/Telephone
Psychological inflexibility and experiential avoidance	AAQ-6	✓	✓	✓	✓	Portal/Telephone Only Portal during intervention
Depressed inactivity	BADS	✓	✓	✓	✓	Portal/Telephone Only Portal during intervention
Fatigue	FSS	✓	✓		✓	Portal/Telephone
Quality of life	EQ-5D	✓	✓		✓	Portal/Telephone
Self-compassion	SCS-SF	✓	✓		✓	Portal/Telephone
Health economics	TiC-P	✓	✓			Portal/Telephone
Acceptability of the intervention; e-therapist; and study procedures; views concerning the impact of the ENGAGE intervention. Non-attendees and poor-attendees are asked about reasons for disengaging, barriers to treatment, and suggestions for future intervention development and study procedures.	Semi-structured questions		✓			Telephone

Note: AAQ-6, Acceptance and Action Questionnaire; BADS, Behavioural Activation for Depression Scale; EQ-5D, EuroQol 5-dimension questionnaire; FSS, Fatigue Severity Scale; FRRS, Fear of Recurrence; GAD-7, Generalized Anxiety Disorder 7-item scale; M.I.N.I, Mini-International Neuropsychiatric Interview; PCL-5 Posttraumatic Stress Disorder Checklist for DSM-5, PCL-C Posttraumatic Stress Disorder Checklist-Civilian version; PHQ-9, Patient Health Questionnaire; SCS-SF, Self-Compassion Scale-Short form; TiC-P, Trimbos and Institute of Medical Technology Assessment Cost Questionnaire for Psychiatry.

Baseline: Participants will be asked to describe their main presenting psychological difficulties and related needs, and expectations concerning the ENGAGE intervention. To inform any future health economic evaluation, they will be asked to describe distressing concerns regarding healthcare utilisation and productivity losses related to their child's cancer disease.

Post-treatment: Parents will be interviewed to explore the acceptability of the ENGAGE intervention and associated study procedures. In order to examine possible mechanisms of change, parents' views concerning the impact of the ENGAGE intervention and CBT techniques had on their mood, and lives more generally, will be explored. The interview guide will be informed by previous research examining the acceptability of CBT self-help interventions [45-47] and qualitative process evaluations.[48] To explore the non-acceptability of the intervention, study procedures, and potential barriers to treatment, non-attendees (parents who do not attend the initial video or telephone assessment session or complete the introductory chapter or any modules) and poor-attendees (attend the initial video or telephone assessment with an e-therapist but disengage prior to completion of the introductory chapter and at least five modules alongside the attendance of the 'booster' support session), will be invited to be interviewed. Semi-structured interviews with non-attendees and poor attendees will explore reasons for disengaging, barriers to treatment, and examine suggestions for future intervention development and study procedures.

Data analyses

Data analyses will primarily be descriptive and will address the outcomes relating to the feasibility of the intervention and study procedures. Progression criteria will be used to determine whether revisions should be considered before proceeding to a controlled trial (Table 2).[22]

Quantitative analyses

An adapted CONSORT diagram for pilot and feasibility studies [23] will be used to illustrate participant flow. Numbers of parents identified via the Swedish Childhood Cancer Foundation and NAVET registry (Swedish Tax Agency) or by advertisements, numbers expressing initial interest, consented, assessed for eligibility, eligible, and included, will be reported. The percentages of: (1) parents assessed for eligibility of the total number invited; (2) parents meeting eligibility criteria of the total number invited; and (3) parents enrolled in the study of the total number invited will be calculated with exact 95% confidence intervals. Reasons for ineligibility, ambiguities regarding eligibility criteria, and reasons for non-participation will be reported at each stage.

Follow-up rates and numbers of missing items relating to outcome measures will be calculated with 95% confidence intervals. In addition, means and standard deviations for the number of reminders sent via text message, e-mail, and telephone will be reported. Potential assessment uncertainties in diagnostic interviews will be reported alongside means and standard deviations for time taken to complete questionnaires and interviews. Descriptive statistics including the means and standard deviations or medians and interquartile ranges and change scores for each outcome measurement at the eligibility interview, baseline, and post-treatment, and at six-month follow-up will be reported. Attrition proportions (both intervention and study dropout) will be reported with 95% confidence intervals.
Means, standard deviations, and frequencies for each Portal activity relating to intervention adherence and use, including logins, opened modules and items, completed action plans and use of optional support functions will be reported. Means, standard deviations, and

frequencies of parent and e-therapist contact within the Portal, via telephone and/or video will be reported and e-therapist adherence measures will be summarised with means and standard deviations and collated in total and by e-therapist.

Means and standard deviations for the length of time taken for parents to work through the intervention and for parents to complete the eligibility interview, baseline, post-treatment (12 weeks), and six months follow-up assessments will be reported. In addition, means and standard deviations will be reported for the length of time e-therapists spend delivering the intervention; for therapist training and supervision, and for project personnel to administer the data collection procedures from invitation through follow-up. This data will be used to assess the feasibility of the intervention and study procedures. Potential ambiguities regarding standard safety procedures, types and numbers of measures undertaken to assure patient safety, and types and numbers of unforeseen safety issues will be reported.

Qualitative analyses

Answers to semi-structured interview questions will be recorded, transcribed verbatim, checked for accuracy, and analysed using qualitative content analysis.[49] To increase trustworthiness of the analysis, at least two researchers and parent research partners will be involved in all stages of analysis to increase credibility, and ensure results accurately represent parents' experiences. Disconfirming case analysis [50] will be conducted to further improve rigour and trustworthiness. Content analysis [51] will be used to analyse the written communication in the interactive functions of the intervention.

Patient and public involvement statement

The intervention and study protocol were designed with input from participants using a participatory action research approach, which was co-facilitated by a member of the research team and a parent of a child successfully treated for cancer [20]. There was no further involvement in the development of this trial by patients or the public, however a patient and public involvement panel will be established to work alongside the research team during the course of the study. An end of study report will be developed to communicate study results to all participants. In addition, a study newsletter will be sent to participants via e-mail approximately six weeks before post-treatment and six-month follow-up.

ETHICS AND DISSEMINATION

The study has been approved by the Regional Ethical Review Board in Uppsala, Sweden (Dnr: 2017/527) and will be conducted in accordance to the Helsinki Declaration, ensuring the welfare and rights of all participants. Confidentiality will be guaranteed and consideration will be given to participants' integrity, dignity, and vulnerability. Informed consent will be collected to ensure participants are aware of the conditions of study participation. Participants will be reminded of their rights to withdraw from the study without giving any reason. Participants will be provided with contact information within the study invitation packs for both the principal investigator (co-author LvE) and the independent Patient Health and Safety Officer for the U-CARE group should they have any cause for concern regarding the conduct of the trial. All data will be handled according to Patient Data Act (2008:355) and the General Data Protection Regulation (EU 2016/679) with all participants assigned a study code to de-identify data and personal information about participants stored separately from de-identified data. Data collected via the Portal will be stored on secure servers at Uppsala University, with personal data and user-generated data stored on separate databases on different servers. The Portal secures de-identification of data and prevents unauthorised persons to connect data from different Portal databases. All other data will be stored in a locked filing cabinet,

accessible only to study personnel. Responsible healthcare provider will be U-CARE Healthcare operating according to the Patient Safety Act (2010:659), Patient Data Act (2008:355) and the Health and Medical Services Act (2017:30). Any adverse events or negative effects discovered during the study will be reported following standard U-CARE Healthcare procedures. Assessments are carried out throughout the study to ensure participants in need of more extensive support, than provided within the study, are identified and guided to appropriate healthcare services. Communication within the Portal will be monitored to identify participants at risk of harm to self or signalling a need for more extensive support. Study findings will be published in an open access journal and via national and international conference presentations.

DISCUSSION

The ENGAGE intervention was developed in response to previous research demonstrating that a substantial subgroup of parents of children previously treated for cancer reports psychological distress in response to their child's disease [3-6] and/or an unmet need of psychological support.[9] Psychological distress related to a child's cancer disease not only cause suffering but also costs to the individual parent.[51, 52] Findings for other populations show that this kind of distress also is costly for society as a whole due to impacts on healthcare utilization and productivity loss.[53] Challenges faced by the Swedish healthcare sector concerning a widening gap between mental health treatment demands and available resources can potentially be addressed using internet-administered interventions supported by cost-effective e-therapists. We have recently published findings demonstrating the clinical effectiveness of an internet-administered psychological, self-help, intervention for parents of children recently diagnosed with cancer.[11, 12] However to the best of our knowledge there is no published evaluation of the clinical efficacy and cost-effectiveness of such an intervention for psychological distress experienced by parents of children previously treated for cancer.

The study presented in this protocol will examine the feasibility and acceptability of ENGAGE, an internet-administered, guided, CBT-based self-help intervention developed to reduce psychological distress among parents of children previously treated for cancer. Investigating the feasibility and acceptability of complex interventions and study procedures is strongly recommended to estimate important parameters and answer key uncertainties required to inform the design of future definitive controlled trials.[54] Given the novelty of the intervention, and limited number of intervention studies conducted with the target population, assessing the acceptability and feasibility of the intervention and study procedures is of great importance in informing intervention refinements and the planning of a future definitive controlled trial. Should the ENGAGE intervention and procedures be demonstrated to be feasible and acceptable, the intervention will be evaluated in a definitive controlled trial. In turn, should the intervention be demonstrated to be clinically and cost effective, the aim is to implement the intervention within the standard Swedish healthcare setting.

Study status: Recruitment is planned to commence during autumn 2018.

ACKNOWLEDGEMENTS

The authors wish to express their gratitude to everyone who has contributed to the development of the intervention and study procedures, especially to the parent and expert research partners and facilitators involved in the development.

AUTHOR CONTRIBUTIONS

Last author LvE conceived the idea for the project and secured funding. LvE and JW developed the methodology and analysis plan with contributions from MC, HG, GL, AR, and AW. LvE, MC, and AW contributed to the development of the intervention. All authors made substantial contributions to the drafting, critical revision, and final approval of the manuscript.

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COMPETING INTERESTS
None declared.

ETHICAL APPROVAL
Ethical approval was granted by the Regional Ethical Review Board in Uppsala, Sweden (Dnr: 2017/527).

SPONSORS
Professor Louise von Essen is the principal investigator and conceived the intervention and the study design and is providing on-going management of the study. The Uppsala University is acting as the study sponsor.

Figure 1. CONSORT-diagram

REFERENCES

1. Gustafsson G, Kogner P, Heyman M. Childhood cancer incidence and survival in Sweden 1984-2010. *Swedish Childhood Cancer Registry* 2013. http://www.forskasverige.se/wp-content/uploads/ChildhoodCancerIncidenceandSurvivalinSweden1984_2010.pdf (accessed 9 November 2017)
2. Pai ALH, Greenley RN, Lewandowski A, et al. A meta-analytic review of the influence of pediatric cancer on parent and family functioning. *J Fam Psychol* 2007;21(3):407-15. doi: 10.1037/0893-3200.21.3.407
3. Wakefield CE, McLoone JK, Butow P, Lenthen K, Cohn RJ. Parental adjustment to the completion of their child's cancer treatment. *Pediatr Blood Cancer* 2011;56(4):524-31. doi: 10.1002/pbc.22725
4. Ljungman L, Cernvall M, Grönqvist H, et al. Long-term positive and negative psychological late effects for parents of childhood cancer survivors: a systematic review. *PLoS One* 2014;9(7):e103340. doi: 10.1371/journal.pone.0103340
5. Ljungman L, Hovén E, Ljungman G, et al. Does time heal all wounds? A longitudinal study of the development of posttraumatic stress symptoms in parents of survivors of childhood cancer and bereaved parents. *Psychooncology* 2015;24:1792–98. doi: 10.1002/pon.3856
6. Bruce M. A systematic and conceptual review of posttraumatic stress in childhood cancer survivors and their parents. *Clin Psychol Rev* 2006;26(3):233-56. doi: 10.1016/j.cpr.2005.10.002
7. Wijnberg-Williams BJ, Kamps WA, Klip EC, et al. Psychological adjustment of parents of pediatric cancer patients revisited: five years later. *Psychooncology* 2006;15(1):1-8. doi: 10.1002/pon.927
8. Steele AC, Mullins LL, Mullins AJ, et al. Psychosocial interventions and therapeutic support as a standard of care in pediatric oncology. *Pediatr Blood Cancer* 2015;62:S585-S618. doi: https://doi.org/10.1002/pbc.25701
9. Kukkola L, Hovén E, Cernvall M, et al. Perceptions of support among Swedish parents of children after end of successful cancer treatment: a prospective, longitudinal study. *Acta Oncol* Published online First: 3 October 2017. doi: 10.1080/0284186X.2017.1374554
10. Wakefield CE, McLoone J, Butow P, et al. Support after the completion of cancer treatment: perspectives of Australian adolescents and their families. *Eur J Cancer Care* 2013;22(4):530–9. doi: 10.1111/ecc.12059
11. Cernvall M, Carlbring P, Ljungman L, et al. Internet-based guided self-help for parents of children on cancer treatment: a randomized controlled trial. *Psychooncology* 2015;24(9):1152-8. doi: 10.1002/pon.3788
12. Cernvall M, Carlbring P, Wikman A, et al. Twelve-month follow-up of a randomized controlled trial of internet-based guided self-help for parents of children on cancer treatment. *J Med Internet Res* 2017;19(7):e273. doi: 10.2196/jmir.6852
13. Stehl ML, Kazak AE, Alderfer MA, et al. Conducting a randomized clinical trial of an psychological intervention for parents/caregivers of children with cancer shortly after diagnosis. *J Pediatr Psychol* 2009;34(8):803-16. doi: 10.1093/jpepsy/jsn130
14. Knowles SE, Toms G, Sanders C, et al. Qualitative meta-synthesis of user experience of computerised therapy for depression and anxiety. *PLoS One* 2014;9(1):e84323. doi: 10.1371/journal.pone.0084323

15. Scott K, Beatty L. Feasibility study of a self-guided cognitive behaviour therapy Internet intervention for cancer carers. *Aust J Prim Health* 2013; 19(4):270-74. doi: 10.1071/PY13025
16. Ferwerda M, van Beugen S, van Burik A, et al. What patients think about E-health: patients' perspective on internet-based cognitive behavioral treatment for patients with rheumatoid arthritis and psoriasis. *Clin Rheumatol* 2013;32(6):869-73. doi: 10.1007/s10067-013-2175-9
17. Craig P, Dieppe P, Macintyre S, et al. Developing and evaluating complex interventions: the new Medical Research Council guidance. *Int J Nurs Stud* 2013;50(5):587-92. doi: 10.1016/j.ijnurstu.2012.09.010
18. Ljungman L*, Cernvall M*, Ghaderi A, et al. An open trial of individualized face-to-face cognitive behavior therapy for psychological distress in parents of children after end of treatment for childhood cancer including a cognitive behavioral conceptualization. *PeerJ*, forthcomming 2018.
19. Kindon S, Kesby M, Pain R. Participatory action research approaches and methods: connecting people, participation and place. 1st ed. New York: Routhledge; 2007.
20. Wikman A, Kukkola L, Börjesson H, et al. Development of an internet-administered cognitive behavioral therapy program (ENGAGE) for parents of children previously treated for cancer: a participatory action research approach. *JMIR,* forthcoming 2018.
21. Eldridge S, Lancaster G, Campbell M, et al. Defining feasibility and pilot studies in preparation for randomised controlled trials: development of a conceptual framework. *PLoS One* 2016;11(3):e0150205.
22. Thabane L, Ma J, Chu R, et al. A tutorial on pilot studies: the what, why and how. *BMC Med Res Methodol* 2010;10:1. doi: 10.1186/1471-2288-10-1
23. Eldridge SM, Chan CL, Campbell MJ, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. *BMJ* 2016;355:i5239. doi: 10.1136/bmj.i5239
24. Moore GF, Audrey S, Barker M, et al. Process evaluation of complex interventions: Medical Research Council guidance. *BMJ* 2015;350:h1258. doi: 10.1136/bmj.h1258.
25. Chan A-W, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. *Ann Intern Med* 2013;158(3):200-7.
26. Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry* 1998;59 (Suppl 20):22-33.
27. Sim J, Lewis M. The size of a pilot study for a clinical trial should be calculated in relation to considerations of precision and efficiency. *J Clin Epidemiol* 2012;65(3):301-8. doi: 10.1016/j.jclinepi.2011.07.011
28. Bower P, Brueton V, Gamble C, et al. Interventions to improve recruitment and retention in clinical trials: a survey and workshop to assess current practice and future priorities. *Trials* 2014;15:399. doi: 10.1186/1745-6215-15-399
29. Barnes M, Wiles N, Morrison J, et al. Exploring patients' reasons for declining contact in a cognitive behavioural therapy randomised controlled trial in primary care. *Br J Gen Pract* 2012;62(598):e371-7. doi: 10.3399/bjgp12X641492
30. Farrand P, Woodford J, Llewellyn D, et al. Behavioural activation written self-help to improve mood, wellbeing and quality of life in people with dementia supported by informal carers (PROMOTE): a study protocol for a single-arm feasibility study. *Pilot Feasibility Stud* 2016;2:42. doi: 10.1186/s40814-016-0083-x
31. Ridgway N, Williams C. Cognitive behavioural therapy self-help for depression: an overview. *J Ment Health* 2011;20:593–603. doi: 10.3109/09638237.2011.613956

32. Farrand P, Woodford J. Impact of support on the effectiveness of written cognitive behavioural self-help: a systematic review and meta-analysis of randomised controlled trials. *Clin Psychol Rev* 2013;33(1):182-95. doi: 10.1016/j.cpr.2012.11.001
33. Barazzone N, Cavanagh K, Richards DA. Computerized cognitive behavioural therapy and the therapeutic alliance: a qualitative enquiry. *Br J Clin Psychol* 2012;51(4):396-417. doi: 10.1111/j.2044-8260.2012.02035.x
34. Weathers FW, Litz BT, Keane TM, et al. The PTSD Checklist for DSM-5 (PCL-5). *National Center for PTSD* 2013. www.ptsd.va.gov (accessed 10 November 2017)
35. Weathers FW, Litz BT, Herman DS, et al. The PTSD Checklist (PCL):reliability, validity, and diagnostic utility. Paper presented at the 9th Annual Conference of the ISTSS. San Antonio (TX); 1993.
36. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001;16(9):606-13.
37. Spitzer RL, Kroenke K, Williams JB, et al. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med* 2006;166(10):1092-7. doi: 10.1001/archinte.166.10.1092
38. Lundgren T, Parling T. Swedish Acceptance and Action Questionnaire (SAAQ): a psychometric evaluation. *Cogn Behav Ther* 2017;46(4):315-26. doi: 10.1080/16506073.2016.1250228
39. Kanter JW, Mulick PS, Busch AM, et al. The Behavioral Activation for Depression Scale (BADS): psychometric properties and factor structure. *J Psychopathol Behav Assess* 2007;29:191-202. doi: 10.1007/s10862-006-9038-5
40. Krupp LB, LaRocca NG, Muir-Nash J, et al. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. *Arch Neurol* 1989;46(10):1121-3.
41. Raes F, Pommier E, Neff KD, et al. Construction and factorial validation of a short form of the Self-Compassion Scale. *Clin Psychol Psychother* 2011;18(3):250-5. doi: 10.1002/cpp.702
42. EuroQol Group. EuroQol--a new facility for the measurement of health-related quality of life. *Health Policy* 1990;16(3):199-208.
43. Bouwmans C, De Jong K, Timman R, et al. Feasibility, reliability and validity of a questionnaire on healthcare consumption and productivity loss in patients with a psychiatric disorder (TiC-P). *BMC Health Serv Res* 2013;13:217. doi: 10.1186/1472-6963-13-217
44. Mitchell N, Hewitt CE, Lenaghan E, et al. Prior notification of trial participants by newsletter increased response rates: a randomized controlled trial. *J Clin Epidemiol* 2012;65(12):1348-52. doi: 10.1016/j.jclinepi.2012.05.008
45. Hind D, O'Cathain A, Cooper CL, et al. The acceptability of computerised cognitive behavioural therapy for the treatment of depression in people with chronic physical disease: a qualitative study of people with multiple sclerosis. *Psychol Health* 2010;25(6):699-712. doi: 10.1080/08870440902842739
46. Farrand P, Woodford J, Small F, et al. Behavioural activation self-help to improve depression in people living with dementia: The PROMOTE treatment protocol. *NZ J Psychol* 2017;46(2):51-62. doi: 10.1186/s40814-016-0083-x
47. Ander M, Wikman A, Ljótsson B, et al. Guided internet-administered self-help to reduce symptoms of anxiety and depression among adolescents and young adults diagnosed with cancer during adolescence (U-CARE: YoungCan): study protocol for a feasibility trial. *BMJ Open* 2017;7(1):e013906. doi: 10.1136/bmjopen-2016-013906

48. Finning K, Richards DA, Moore L, et al. Cost and outcome of behavioural activation versus cognitive behavioural therapy for depression (COBRA): a qualitative process evaluation. *BMJ Open* 2017;**7**(4):e014161. doi: 10.1136/bmjopen-2016-014161
49. Graneheim UH, Lundman B. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. *Nurse Educ Today* 2004;24(2):105-12. doi: 10.1016/j.nedt.2003.10.001
50. Patton MQ. Qualitative evaluation and research methods. 2nd ed. Newbury Park (CA): Sage; 1990.
51. Mader L, Roser K, Baenziger J, et al. Household income and risk-of-poverty of parents of long-term childhood cancer survivors. *Pediatr Blood Cancer* 2017;64(8). doi: 10.1002/pbc.26456
52. Lindahl Norberg A, Montgomery SM, Bottai M, et al. Short-term and long-term effects of childhood cancer on income from employment and employment status: a national cohort study in Sweden. *Cancer*, 2017;123(7):1238-48. doi: 10.1002/cncr.30436
53. Smit F, Cuijpers P, Oostenbrink J, et al. Costs of nine common mental disorders: implications for curative and preventive psychiatry. *J Ment Health Policy Econ* 2006;9(4):193-200.
54. Eldridge SM, Lancaster GA, Campbell MJ, et al. Defining feasibility and pilot studies in preparation for randomised controlled trials: development of a conceptual framework. *PLoS One* 2016;11(3):e0150205. doi: 10.1371/journal.pone.0

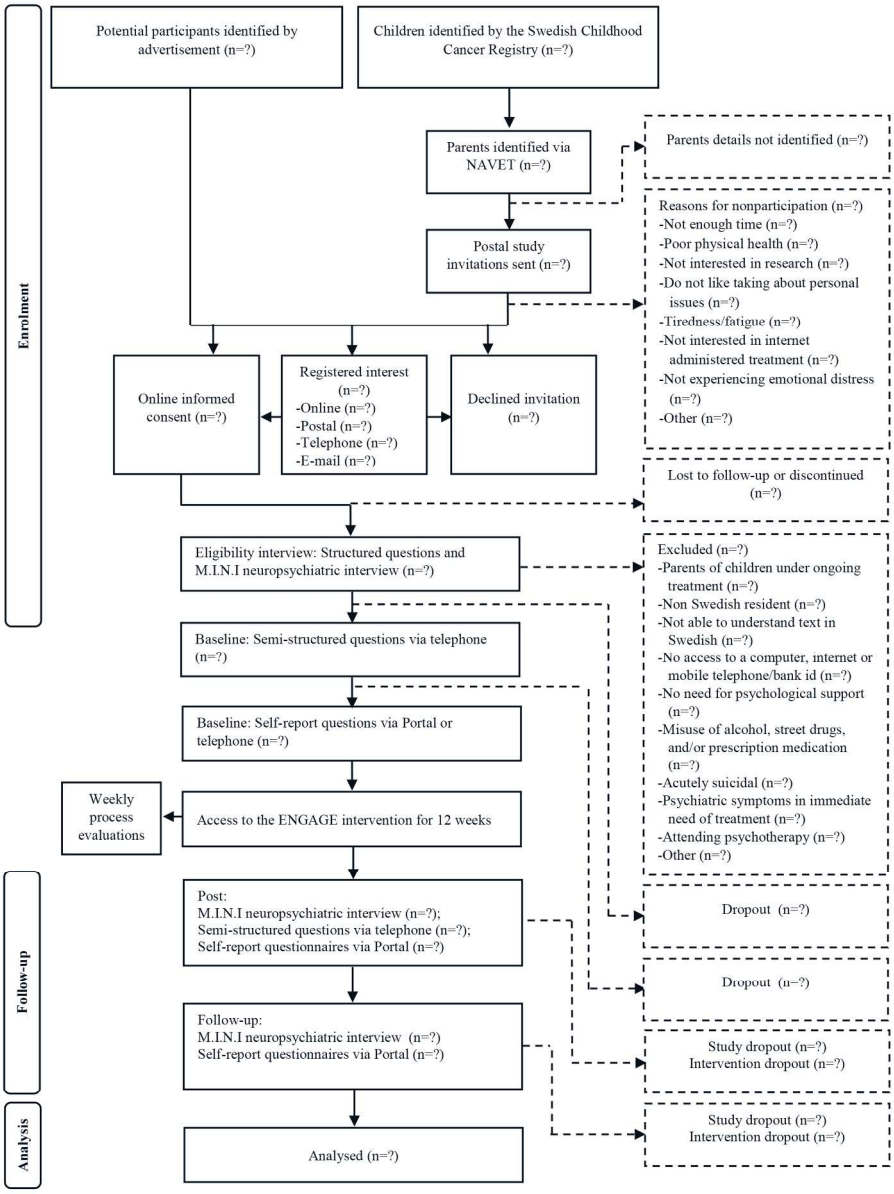

Figure 1. CONSORT-diagram

176x232mm (300 x 300 DPI)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

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		Reporting Item	Page Number
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	Throughout
Protocol version	#3	Date and version identifier	5
Funding	#4	Sources and types of financial, material, and other support	19
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1, 18
Roles and	#5b	Name and contact information for the trial sponsor	19

responsibilities: sponsor contact information			
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	19
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N.A
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	N.A
Objectives	#7	Specific objectives or hypotheses	5
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	5
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	10
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	5, 7, 9

Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7-10 Table 1 (8)
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	N.A
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	13
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	5
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	10-15 Table 2 (11-12) Table 3 (14-15)
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	6-7 Figure 1
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	5-6
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	6
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned	N.A

		restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	N.A
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	N.A
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	N.A
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N.A
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	10-16 Figure 1 Table 2 (11-12) Table 3 (14-15)
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	6, 13, 16
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	17

Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	16-17
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	N.A
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	N.A
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	N.A
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N.A
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	N.A
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N.A
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	1, 17, 19
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	N.A

Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	6, 7, 17
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N.A
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	17
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	19
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	N.A
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N.A
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	17
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	N.A
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	N.A
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	N.A
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future	N.A

use in ancillary studies, if applicable